Showing RESPECT:

a mixed methods study into communicating the results of a Phase III clinical trial to trial participants

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Institution: **UCL**

Degree for which the thesis is submitted: **Doctor of Philosophy in Clinical Trials Methodology**

Declaration

I, Annabelle Eileen South, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Abstract

Introduction

Clinical trials depend on volunteers participating, often accepting increased risk and/or inconvenience. Most participants want to receive the results of trials they have participated in, while few actually receive them. There is little evidence to guide researchers on how best to share results with people taking part in trials.

Methods

I conducted a mixed methods, cluster randomised factorial trial of different approaches to sharing results with participants in the ICON8 ovarian cancer trial. (ICON8 tested two weekly chemotherapy schedules against the standard three-weekly schedule, and found no difference between the arms). I collected quantitative and qualitative data from patients and site staff.

Results

Patients at hospitals that were randomised to the Posted Printed Summary were more satisfied with how the results were shared and more likely to find out the results than those at hospitals not randomised to the Printed Summary. Women who received the results said that the information was easy to understand and find, and told them everything they wanted to know. Most were glad to receive the results, and did not regret finding them out, although some were, at the same time, disappointed that ICON8 interventions did not improve outcomes. This links back to their motivation for joining the trial: to benefit themselves and future patients.

Site staff were supportive of sharing results with participants, seeing it as a way of respecting and valuing participants, and repaying trust. Staff at most sites found the process used to share results straight-forward and not too time-consuming. Sharing results by post increased site costs by ~£14 per participant.

Conclusion

My findings can inform how future trials share results with participants, helping improve participants' trial experience. Further research is required to look at how different patient populations, trial results and settings influence participant satisfaction with how results are shared.

Impact Statement

Improving participants' trial experience

My qualitative results show that communicating trial results to participants well can make the trial experience feel more worthwhile, provide closure, and help ensure participants feel valued. As the results from Show RESPECT have impact on the conduct of future trials, I hope it will help improve the trial experience for participants.

Increasing knowledge

The Show RESPECT study is the first randomised controlled trial to compare different ways of sharing results with trial participants. It provides high quality evidence to guide practice, and incorporates evidence on the views of site staff and participants, and information on the feasibility of implementing the interventions as well as their effectiveness.

My primary target audience for the results of Show RESPECT is people involved in running randomised controlled trials. My communication efforts to reach this audience include posters and presentations at international conferences and seminars at several clinical trials units. The patient results were published in a high profile Open Access journal (PLoS Medicine), which has so far had more than 2,000 reads. I have produced an episode of the MRCCTU at UCL podcast, aimed at trialists, exploring the importance of sharing results with participants which has had more than 400 listens. Another episode, focusing on how to share results with participants, will be released soon.

I was part of a panel discussion on sharing results with participants at the Health Research Authority Research Transparency Conference in 2021. The audience for this included researchers, funders, ethics committee members and patient advocates.

The main results of Show RESPECT have been shared with ICON8 participants alongside the long-term ICON8 results, in a posted printed summary.

The Show RESPECT study has demonstrated that high quality studies within trials can be carried out to look at how to communicate results to participants. The protocol for Show RESPECT is available online, allowing others to see how the study was carried out, and adapt it for other randomised controlled trials. Researchers at McGill University in Canada have put in a grant application to run a series of randomised controlled trials testing different approaches of communicating trial results to patients, informed by Show RESPECT.

Informing practice

I have been part of the Health Research Authority working group developing guidance on communicating trial results to participants for trials across the UK, informed by Show RESPECT. This guidance is due to be released soon, and is likely to be very influential, given the role the Health Research Authority plays governing the conduct of clinical trials in the UK.

Cost results from Show RESPECT have also helped inform forthcoming updated funding guidance from Parkinson's UK, who are changing their rules to allow applicants to include the costs of communicating with participants in grant applications.

Based on my research I have developed practical recommendations to guide triallists, available on the MRCCTU at UCL website. They are informing new MRCCTU at UCL guidance on communicating results to trial participants.

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“Plans fail for lack of counsel, but with many advisers they succeed.”

(Proverbs 15:22)

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Show RESPECT was a trial, and, like all trials, depended on ‘team science’ for success. Thanks to Will Cragg, Conor Tweed, Cara Purvis and Andrew Copas for helping me to develop the Show RESPECT protocol. Thanks to the Show RESPECT Study Management Team for their work, dedication and skill in making this study successful: Cara Purvis, Nalinie Joharatnam-Hogan, Archie Macnair, Sierra Santana, Ania Spurdens, Carlos Diaz-Montana and Andrew Copas. Thanks also to Liz James, who double programmed the primary endpoint of the study, and assisted in the randomisation process. Show RESPECT benefited from a wise, engaged Steering Group, who have helped me to articulate the study findings more clearly, and encouraged me to stay true to the mixed methods design of the study, when the temptation was to write up the quantitative and qualitative components separately. The Steering Group included: Katie Gillies, Claire Snowdon, Talia Isaacs, Barbara Bierer, Eva Burnett, Matt Sydes, Liz James and Amanda Hunn. Thanks also to the ICON8 team for their support of this research, including Andrew Clamp, Rick Kaplan, Babasola Popoola, Jonathan Badrock, Francesca Schiavone, Liz James and Adrian Cook.

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Thanks also to my husband Chris South, my family and friends for their support and encouragement.

Abbreviations

A-level	Advanced level
AMRC	Association of Medical Research Charities
AVAC	Global Advocacy for HIV Prevention organisation
CISCRP	Center for Information and Study on Clinical Research Participation
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CTU	Clinical Trials Unit
EU	European Union
FAQ	Frequently Asked Questions
FIGO	International Federation of Gynecology and Obstetrics
GCSE	General Certificate of Secondary Education
GP	General Practitioner
HIV	Human Immunodeficiency Virus
HRA	Health Research Authority
ICC	Intracluster Correlation Coefficient
ICON8	An international Phase III randomised trial of dose fractionated chemotherapy compared to standard three weekly chemotherapy, following immediate primary surgery or as part of delayed primary surgery, for women with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancer
IRAS	Integrated Research Application System
ISCM	Information-Seeking and Communication Model
IT	Information Technology
IV	Interviewer
mITT	Modified Intention to Treat
MRCCTU at UCL	Medical Research Council Clinical Trials Unit at University College London
MRCT	Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard
MREC	Medical Research and Ethics Committee
NHS	National Health Service
NIHR	National Institute of Health Research
NVQ	National Vocational Qualification
O-level	Ordinary level
OR	Odds ratio
PhD	Doctor of Philosophy
PLoS	Public Library of Science
PPI	Patient and Public Involvement

PROUD	PRe-exposure Option for reducing HIV in the UK: an open-label randomisation to immediate or Deferred daily Truvada for HIV negative gay men
PUIS	Patient Update Information Sheet
RCT	Randomised Controlled Trial
RECAP	REporting Clinical trial results Appropriately to Participants
Show RESPECT	Show Results to Participants Engaged in Clinical Trials
TIDIER	Template for Intervention Description and Replication
UCL	University College London
UK	United Kingdom
UKRI	United Kingdom Research and Innovation
UNAIDS	Joint United Nations Programme on HIV/AIDS
URL	Uniform Resource Locator
USA	United States of America

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1. Communicating results of randomised controlled trials to participants: considerations and the current evidence base

1.1 Randomised controlled trials

Randomised controlled trials are considered the 'gold standard' approach to establishing the efficacy and safety of new interventions[1]. They do this through randomising participants to either the new intervention or a control, which may be the current standard of care, a placebo, or no intervention. Participants are followed up and outcomes collected in the same way from both groups, which allows fair comparisons to be made. Phase III trials are randomised controlled trials comparing the new intervention to the standard of care. Earlier phase trials (Phase I and II) are not usually randomised, and may have no control arm, or the control arm may be no treatment or placebo, rather than standard of care. Evidence from Phase III trials is required by drug licensing authorities before a new treatment is approved, as it is at this stage we learn whether the intervention is effective compared to existing approaches.

The roots of clinical trials go back to the eighteenth century, with James Lind's experiments of different treatments for sailors with scurvy[2]. The UK Medical Research Council were the first to report results from a rigorous randomised controlled trial, from their 1947-48 trial testing streptomycin for the treatment of tuberculosis[3]. The RCT method was gradually adopted in the UK, with their use expanding rapidly in the USA and elsewhere following changes to legislation in 1970 which required data from controlled clinical trials in order for drugs to be licensed[2]. While the design of randomised controlled trials has developed over the years, with the introduction of approaches including factorial designs, cluster randomisation, multi-arm, multi-stage design and other adaptive platform approaches, the fundamentals of random allocation between intervention(s) and control groups remain the foundation for evaluation of new interventions.

Phase III randomised controlled trials often require hundreds or thousands of participants to detect meaningful differences in outcomes. This means they can be costly, and may take years to carry out[4]. In order to successfully answer the question they set out to, trials must recruit volunteers to take part, often asking participants to accept increased risk. For example, the risk that the intervention may be less effective than the standard of care or have increased side-effects. Trials may require participants to undergo additional tests, scans and/or clinic visits, with associated inconvenience, discomfort and

cost. Trials within the UK National Health Service may involve staff from many different disciplines, across many different sites. All this effort aims to improve treatment, care or disease prevention for future patients.

According to the World Health Organisation Global Observatory on Health Research and Development, almost 6,000 Phase III clinical trials took place in 2021 globally[5]. This is up from just over 500 registered Phase III trials in 2000. The UK hosted around 11% of Phase III trials globally in 2021, with cancer trials making up more than a quarter of UK Phase III trials. Most of these trials aimed to recruit between 101 to 1000 participants. There were 6 Phase III ovarian cancer trials taking place in the UK in 2021[5].

1.2 Aims and audiences for communicating the results of Phase III randomised controlled trials

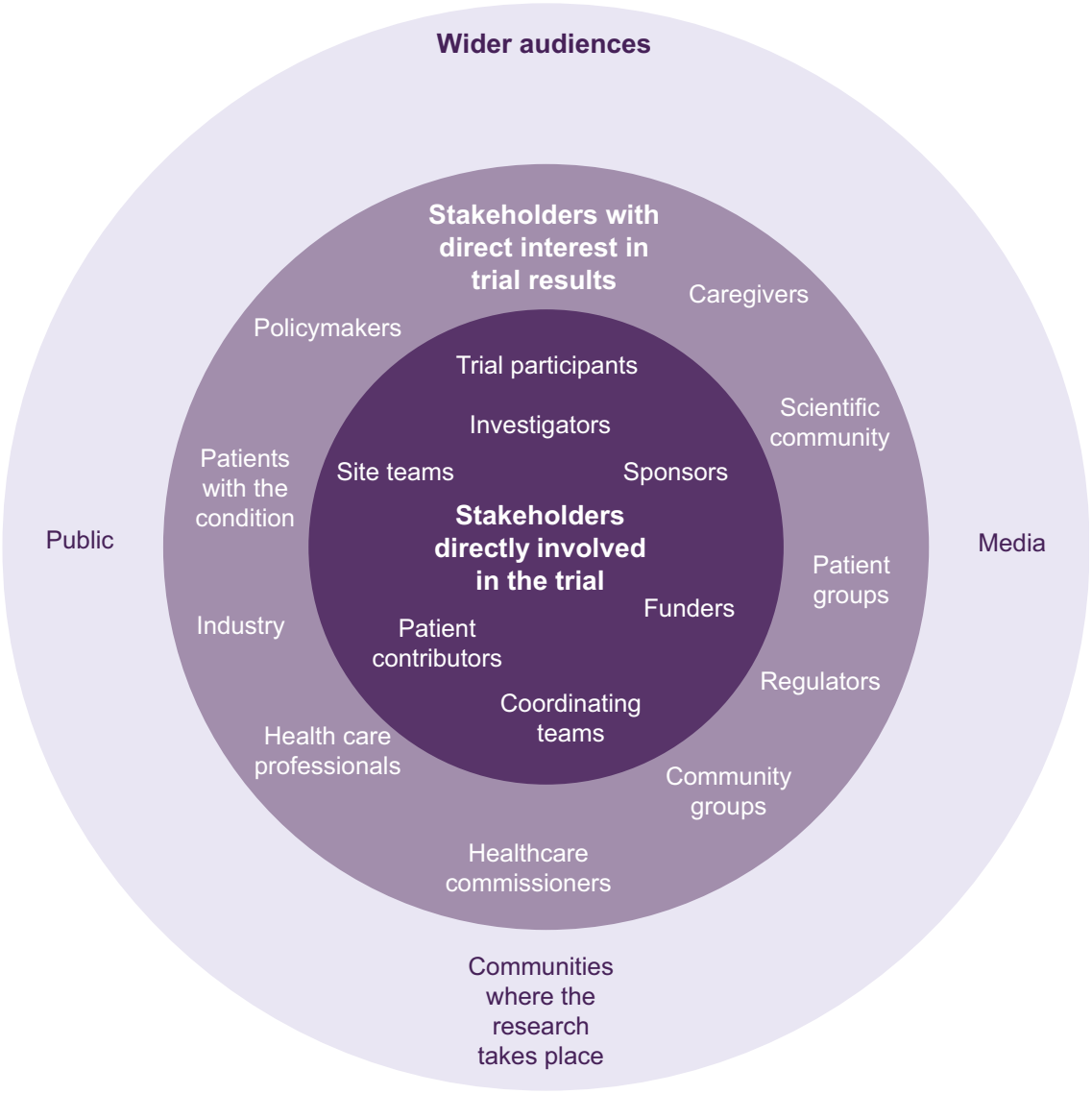
Communication of trial results is important for a number of reasons, including:

- informing policy and practice
- increasing transparency around research results to ensure the evidence base is not biased by selective reporting[6]
- improving trust in research
- reducing research duplication and waste
- increasing awareness of the importance of clinical trials among potential research funders (including, ultimately, tax payers and people who donate to medical research charities), participants and collaborators

These different aims of communication suggest a number of different audiences for trial results. These audiences range from those closely involved in the study, through to those who may never have heard of it, as illustrated in Figure 1.1. In a separate piece of work, I have conducted a systematic review looking at how trial results are communicated to professional audiences, including healthcare workers and policymakers. This PhD focuses on the communication of trial results to those most directly affected by the trial: the people taking part in it. These are the audience with the most at stake, having taken part in a trial often at the expense of extra risk and inconvenience.

This PhD focuses on the return of overall trial results (e.g. whether the intervention was superior to control on average) to participants, rather than an individual participant's results (e.g. personal results from any test procedures carried out on them as an individual). These two types of results communication have different practical and ethical considerations. In some trials, participants receive the results of scans and tests carried

Figure 1.1: Audiences for the results of randomised controlled trials



out on them from their clinicians as the trial proceeds, while in others this information may not be available normally, if carried out for research rather than clinical management purposes. There is less agreement on the need to communicate individual results, so these are best considered separately[7]. The communication of individual results is beyond the scope of this thesis.

1.3 Why communicate with trial participants?

Sharing results with people who have taken part in trials is an ethical imperative[8], and is recommended by authorities that govern the conduct of clinical trials. Fernandez et al argue that the principle of respect, which is central to ethical research conduct, should extend to informing trial participants of research results at the end of the study, in order to avoid treating participants as just a means to an end[9]. The World Medical Association's Declaration of Helsinki, which outlines the principles for ethical conduct of

medical research involving human participants, states "All medical research subjects should be given the option of being informed about the general outcome and results of the study"[10]. The Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials state that "Research teams [should] ensure that trial participants are provided opportunities to learn trial results before they are announced publicly"[11]. In the UK, the Health Research Authority (HRA) introduced guidance in 2015 recommending that all researchers offer trial results to participants[12].

There is evidence from studies conducted in a range of diseases (cancer, idiopathic scoliosis, internal derangement of the knee, HIV) and geographical settings (USA, UK, Canada and Uganda) that most participants (88-98%) want to be offered the opportunity to receive trial results[13-17].

Offering results to trial participants is purported to have other benefits, besides demonstrating respect or appreciation for participants' contribution. These benefits include:

- Reducing the likelihood of participants feeling exploited by the researchers[9]
- Providing information that may be of use to participants for their health in the future[9]
- Increasing awareness of the impact and importance of clinical trials[9]
- Enhancing trust in the research process[9]
- Increasing the likelihood of participants agreeing to take part in future research[13, 18-21]
- Increasing the likelihood that participants will recommend taking part in research to others[13, 18-21]
- Improving participant satisfaction with care or quality of life[22]

Not offering results to people taking part in trials runs the risk of undermining trust in clinical research, making people feel used and less likely to agree to be part of research in the future[23].

1.4 To what extent are trial results shared with participants currently?

Despite the ethical imperative and clear demand from participants and funders for sharing results, in practice it often does not happen, or is not done well. The UK Health Research Authority research transparency report from 2021 stated that "90% of clinical trials have not told participants about findings"[24]. A survey, carried out in 2016, of authors of clinical trial results papers published in 2014-15 found that only 27% of respondents reported disseminating results to participants, with a further 13% planning to do so[25]. This is likely

to be an overestimation, as the response rate to the survey was low, and it is plausible that non-responders may have been less likely to have shared results with participants. Little seems to have changed in practice since 2004, when researchers in the US found that most oncology physicians and nurses offered trial results to participants less than one fifth of the time[22].

These continued low figures contrast with the results of an audit of records of clinical trials submitted from 2012-17 to the Integrated Research Application System (IRAS), which is the system for gaining health research approval in the UK. According to these records, 88% of Phase III clinical trials stated that they intended to disseminate results to participants, with 19% of these trials intending to use an active dissemination approach (where the trial team directly inform participants how to access results) and 81% of them planning to use passive dissemination approach (where trial team do not directly inform participants of how to access results)[26]. It is unclear whether this gap between stated intention, and observed practice are a result of the trials in the IRAS dataset not having produced results to share yet, or whether researchers' intentions do not translate into action when results are available. There does seem to be increasing interest in sharing results with participants among the academic community, with a recent scoping review finding that 70% of the studies of sharing results with participants identified for inclusion were published between 2010-2019[27]. However, it is likely that there is still a considerable gap between participants' desire to know trial results, and the opportunities they are offered to receive them.

1.4.1 Motivation to do this study

My interest in this as a research topic came from an encounter I had with a participant in one of the trials I had been involved in communicating. The trial had produced results, we had written a summary for participants, in plain English and nicely presented, with input from patient representatives. These summaries were then professionally printed, and sent out to each of the hundred or so sites, with investigators asked to share them with participants. Around six months later I met a participant who said he had been on the trial for years, and no-one had ever offered him the results. He was angry and upset about this. Clearly the process we were using for sharing study results was not working perfectly. I discussed this encounter with my counterparts at Cancer Research UK. It chimed with the results of a survey they had recently conducted, which showed that many cancer trial participants were unhappy that they never got to learn the results of the trials they had taken part in. We decided to explore this more, through patient and public involvement (PPI) and reviewing the literature, which eventually led to the design of this study.

1.5 What inhibits communication of results to participants?

There are many barriers to the communication of results, including practical challenges; concern about the impact of sharing results; uncertainty about how to do it; it not being mandated by funders[25] or ethics committees[28-30]; lack of guidance[25, 31]; lack of incentives[25]; concern about compromising commercial interests[32, 33]; participants' perceived lack of interest[25, 34, 35] or ability to understand results[9, 22, 25, 31]; or researchers simply not thinking about it[28]. Trialists may also encounter challenges with complying with ethics committee and regulatory rules, for example around avoiding the use of language that may be seen as promotional[32, 33], or if communication of results to participants had not been part of the original ethics application[25].

1.5.1 Practical challenges with sharing results with participants

Cost is a major barrier to sharing results with participants, with many trials not having budgeted for this activity[25, 30, 32, 34, 36, 37]. Linked to this is the issue around the staff time required for sharing results, which often occurs at a point where staff may have already been moved to work on new trials, leaving little human resource for this activity[25, 35-37]. Another practical challenge is the difficulty in contacting patients, when results may come out several years after their follow-up has finished, meaning contact details may be out of date[25, 28, 32, 35-37], or their wishes around whether to receive results may have changed, which needs to be tracked[32]. The question of when results should be shared (prior to presentation at a scientific conference, at the same time as presentation, between presentation and publication or after publication) is also an area of uncertainty for trialists[31, 32]. In some trials, Sponsors (the organisation responsible for the trial) may not have any direct contact with participants, leaving them reliant on busy clinical sites to share results[32]. Another practical barrier to sharing results may be lack of the skills required to communicate results intelligibly and sensitively to participants[25, 31, 32, 35, 36]. The need to provide results in multiple languages may also be a challenge[25]. Maintaining patient confidentiality and complying with data protection laws may also pose challenges to sharing results[25, 32].

1.5.2 Concern about the impact of sharing results with participants

Researchers may be reluctant to share results with participants due to concern about the impact this may have on them, particularly if the results are perceived as negative, harm was seen in the trial, or the participant was in the inferior arm, all of which could be upsetting[13, 16, 19, 22, 34-36, 38, 39]. Linked to this is the concern that sharing results with participants could be upsetting for trial staff as well[35]. There is also the possibility that participants may have

died, and, if results are sent to them by accident, this could be distressing for their families[16, 32, 34]. Another cause of reluctance to share results with participants is concern that it may bias further follow-up, if participants are still being followed for longer-term outcomes when the first results are available[32, 38].

1.5.3 Uncertainty about how to share results with participants

Sharing results with participants is not straightforward, creating uncertainty about how best to do it. Part of this complexity is around the diverse needs of participants, who may have limited access to or understanding of technological approaches such as webpages, apps or email[25, 32]. Participants may also have low literacy, meaning communicating complex results may be difficult for researchers[31, 32, 40]. Section 1.6 outlines the evidence on different approaches to sharing results with participants.

1.6 Approaches to communicating results to participants

There are a wide variety of approaches that could be used to communicate results to participants, but the evidence base to support any of these is weak. Most of the evidence is based on surveys of participants or the public, prospectively asking how they would prefer to be informed, or retrospectively asking whether an approach that was used was acceptable or understandable, rather than systematically comparing outcomes from different approaches[13, 14, 16, 18-20, 37, 39-45]. The evidence around the main approaches that are reported in the literature (printed results sent by post, webpages and email, and two-way communication approaches) is summarised in the rest of the section.

1.6.1 Printed results sent by post

Most of the published evidence to date relates to sharing results with participants via posted letters or leaflets; these studies generally report high acceptability of this approach[13-15, 19, 20, 37, 42, 43, 45-47]. However, sending out results by post has resource implications, which could be substantial for very large trials. There are increasing moves towards electronic means of communication, such as webpages and emails, which may be less costly to implement.

1.6.2 Webpages and email

Sharing results via webpages has a number of potential advantages, including the ability to offer links to further information or support, include audio and visual content alongside written summaries, and being discoverable

by participants who have been lost to follow-up. There are also potential drawbacks in terms of accessibility for populations with low computer literacy. Fewer studies have reported sharing results via webpages than by post. One study randomised participants in a breast cancer trial to receive a letter containing a link to a website with the trial results, or no letter. They found that participants who received the letter had better understanding of the results, but were not significantly more likely to have received the trial results than participants who did not receive the letter[48]. Other studies have reported low uptake of results shared via webpages[42, 43], or lower levels of satisfaction with how the results were shared[45]. There is less evidence around the use of email to share results with participants, however one study found that potential research participants would be happy to receive results that way[41], and it was the preferred approach in two surveys of cancer patients in the USA because it is seen as quick and easy for both researchers and participants[49].

1.6.3 Two-way communication approaches

Other approaches to sharing results include face-to-face meetings[40, 43, 45], teleconferences[44] and individual telephone calls or helpline services[13, 44, 46]. These approaches facilitate two-way dialogue, allowing participants to ask questions and seek clarification. However, the resource requirements for these approaches may be prohibitive, particularly for large trials, and uptake of these services may be low, with Dixon-Woods et al reporting no calls to a telephone helpline[46].

1.7 How do participants respond to receiving trial results?

A wide variety of outcomes have been measured in studies of sharing trial results with participants. The most common of these outcomes are preferred mode of communication, comprehension of the results, demand for or uptake of results and reaction to the results. Other, less commonly reported outcomes include satisfaction with communication, whether participants would recommend taking part in research to others, participants' need for support following receipt of results, and quality of life upon learning the results.

Generally, participants' response to receiving trial results seems to be positive[37, 43, 44, 46, 50, 51]. Several studies report participants gaining pleasure from receiving results[16, 25, 37, 52, 53]. 96% of respondents in a study among people with myocardial infarction said they were pleased to have been informed, found the results interesting, relevant and easy to understand[43]. Similarly, 96% of women in a breast cancer trial were glad to have been offered the results, and 95% of those who received the results did

not regret their decision[13]. A case study of using a meeting to share results with participants in a prospective cohort study in rural Uganda found that the event helped make the participants feel respected, and created a sense of community among participants[17]. 95% of participants in a long-running cataracts trial would recommend taking part in clinical trials to others[20], while 89% in a Phase III breast cancer trial[19] and 70% in a Phase II breast cancer trial that was stopped early due to a negative result would recommend participation to others[13].

Studies show that it is possible to create comprehensible results summaries for participants. Some studies have reported 84%-98% of participants saying results summaries (some developed with extensive PPI) were easy to understand[13,37,51], while others report around 57-63% saying they understood the results very well, or the summaries were very clear[42,20].

While there are reports in the literature that receiving study results may be upsetting for some participants in some circumstances (e.g. if they were in the group that did less well on the trial, or if they had experienced side-effects) [16, 37, 43, 46, 47], that does not necessarily mean that they would be better off not having received the results[54]. This echoes what was found in a study of parents of babies in a trial; although receiving results may be upsetting, that does not mean they would rather not have received them[47, 55].

1.8 What should be communicated?

Various guidance has been issued around what should be included in a summary of results for lay audiences in general, or trial participants specifically. Table 1.1 summarises guidance from the Multi-Region Clinical Trials Center (MRCTC) issued in 2015[56]; the 2017 version of the MRCTC guidance document[57] (updated based on the European Parliament Regulation (EU) No 536/2014 Article 37 (4) requirements on content of lay summaries of results of clinical trials[58]); and the Center for Information and Study on Clinical Research Participation (CISCRP) structure for results summaries[59]. CISCRP is a non-profit organisation that works with pharmaceutical companies to develop participant summaries of trial results. There is considerable overlap between the three results summary structures, although the exact heading names and what is included under them differs. The order of headings differs, for example the position of the summary of results varies from being the third item in the MRCTC 2015 guidance, to 8th item in the 2017 version, and 6th in CISCRP structure. The MRCTC 2017 guidance includes sections on who sponsored the study, and who took part in the study, which are not standalone sections in the other guidance. It also includes plans for further studies, which

is not explicitly included in the other guidance. The CISCRP structure includes a section on what is happening in the trial now, which is not part of the other summaries (which may assume the study has finished).

Table 1.1: Information items recommended to be included in results summaries for participants in different guidelines

MRCTC 2015	MRCTC 2017	CISCRP
A thank you to study participants	*A thank you to study participants*	*Thank you message to volunteers*
Simple title of the study	Study name (simple version + *full version for UK studies*)	What is happening with the trial now?
Summary of results	*Who sponsored this study*	Why was the research needed?
Why the study was done	General information about the clinical trial (dates, countries, why it is important, purpose)	What treatments did the patients take?
Study information (dates, countries, study population)	What patients/people were included in this study?	What happened during the trial?
How the study worked	What medicines [or vaccines] were studied?	**What were the results of the trial?**
Safety events	**What were the side effects?**	**What medical problems did the patients have?**
Official title of the study	**What were the overall results of the study?**	**How has this trial helped patients and researchers?**
Final comments (whom to contact with questions, *study ID numbers*, where to find further information, *sponsors*)	**How has this study helped patients and researchers?**	Where can I learn more?
	Are there plans for further studies?	
	Where can I find more information about this study?	

Key:

Bold text used to indicate items identified as most important by respondents considering an individual view in the RECAP study (see Table 1.2);

Purple text used to indicate items identified as most important by those considering an population view in the RECAP study;

Italic used to indicate items identified as least important from an individual view in the RECAP study;

Underline used to indicate items identified as least important from a population view in the RECAP study.

The RECAP study explored which information items are most important to include in results summaries for participants. The researchers interviewed a mix of trial professionals and patients and the public, asking them to rank information items that might be included in the results summary of a trial. They found two different points of view on what was most and least important in a results summary, split by whether the interviewee was taking a population view or considering it as an individual (Table 1.2)[60]. The items identified as most important by those considering the question from an individual view are shown in bold in Table 1.1, and those identified as most important by those taking a population view are indicated with purple text. Those deemed least important from an individual view are shown in italic in Table 1.1, and those deemed least important from a population view are indicated with underlining. The 'primary outcome' item is not a specific heading in any of the structures, but is likely to be included in the sections on how the study worked, its purpose or within the results section. In two of the three structures, the first of the most important information items from an individual view comes at least halfway down the list. In the case of the MRCTC 2017 guidance, this is after four items that are viewed as least important from a population or individual level perspective. This suggests that the current structures may not be well aligned with the priorities of key stakeholders in the process. The CISCRP structure includes the fewest items identified as least important from either perspective.

Table 1.2: Most and least important information items identified in the RECAP study[60]

	Population view	**Individual view**
Most important items	A thank you message	Primary outcome
	Clinical implications of the results	Clinical implications of the results
	Topline overview of study results	What were the side-effects?
Least important items	Sponsor details	A thank you message
	Trial identifier and full title	Sponsor details
	General information about the trial – administrative information	Trial identifier and full title

1.9 Making results understandable

There is little point to providing results to participants if the information is provided in a way that is incomprehensible to lay audiences. Doing this could potentially lead to confusion or misinterpretation, which could be harmful. In order to create summaries of trial results that are understandable by participants, researchers need to consider the health literacy and numeracy of the participant population and employ the principles of writing in plain language and good risk communication. How the information is framed will also make a difference to how it is interpreted, while the visual presentation of

the information can help or hinder comprehension. This section explores each of these issues in turn.

1.9.1 Health literacy and numeracy

Health literacy can be defined as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health"[61]. Health literacy is dependent on literacy, which, according to the National Literacy Trust, is "the ability to read, write, speak and listen in a way that lets us communicate effectively and make sense of the world"[62]. Around one in six people in the UK are functionally illiterate, which means that reading information from unfamiliar sources, or on unfamiliar topics, is difficult for them[63]. Health information is often from unfamiliar sources for most people, or on unfamiliar topics, and many people have difficulty understanding health information[64, 65]. It is therefore important that trial results summaries are written in a way that is easy to understand for people with limited literacy skills.

Numeracy is the ability to understand quantitative or numerical information[66], and health numeracy can be defined as "the degree to which individuals have the capacity to assess, process, interpret, communicate and act on numerical, quantitative, graphical, biostatistical and probabilistic health information needed to make effective health decisions"[67]. Health numeracy, alongside health literacy, is necessary to understand much health information, including trial results. There is often a substantial mismatch between the levels of health literacy and numeracy needed to understand health information materials, and average levels of health literacy and numeracy in the UK[68]. How researchers present numerical aspects of trial results can make a substantial difference to the understandability of those results.

1.9.2 Principles of writing in plain language

Plain language is "writing that is clear, concise, well-organised, and follows other best practices appropriate to the subject or field and intended audience"[69]. Using plain language may help improve understanding of written information, even among people with higher levels of health literacy[70, 71], and may also be more acceptable and useful to the target audience[72]. However, the size of the effect may be marginal[73]. In the UK, the National Health Service Digital Service Manual style guide states that they aim for a reading age of 9-11 years old where possible[74]. The general principles of writing in plain English include writing with the audience in mind; using everyday language where possible (and defining more complex, specialist terms where needed); preferring short words to longer alternatives; using short

sentences and paragraphs; using the active rather the passive voice where possible; and avoiding nominalisations (abstract nouns)[75]. This may be challenging for medical information, where jargon is common and accuracy vital. However, if our aim is to communicate trial results to trial participants, who are generally not medical experts, in a way they can understand, we need to be careful about the language we use to maximise clarity. Employing the principles of writing in plain language may help with this.

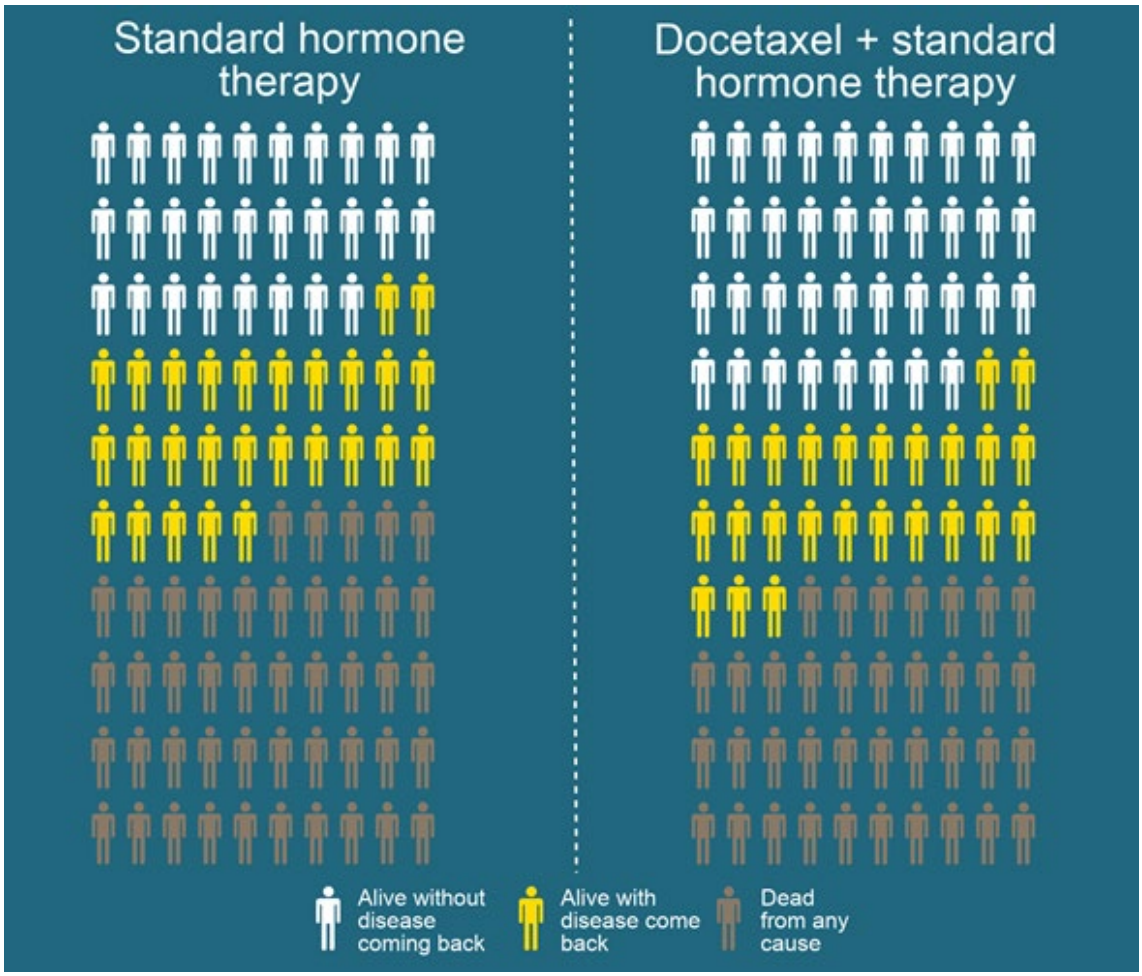
1.9.3 Approaches to presenting risk

The results of clinical trials are often presented in numerical forms such as percentages, frequencies, risk, odds or hazard ratios, or numbers needed to treat. They can also be expressed using words such as 'likely' or 'rare'. The way in which risks are presented in results summaries for participants is likely to affect both comprehension and interpretation of that information[66, 76]. Percentages may be most likely to support comprehension among highly numerate younger adults and healthy older adults when comparing percentages above 1%[66]. Natural frequencies (e.g. 5 out of 100) are an alternative approach to presenting the information, which may make it easier for people to interpret[77], providing the denominator remains constant to allow easy comparison (it is easier to compare 5 in 100 vs 4 in 100 than 1 in 20 vs 1 in 25). Adding verbal terms (such as "common") alongside numerical risks lead to overestimation of risks compared to giving the information as numerical frequency bands alone (contrary to EMA guidance)[78]. Verbal terms for likelihood are problematic because they are interpreted differently by different people[79]. Absolute risk reduction is better understood than relative risk reduction[77], which can lead to an overestimation of intervention effects[79]. Patients presented with information about the effectiveness of statins presented in 'prolongation of life' (the extra length of life on average that people taking statins can expect) format in a study were less likely to redeem a statin prescription than if given the information as absolute risk reduction[80].

There are many approaches to presenting risk visually, including bar charts, pictographs, line graphs and pie charts. More complex graphical formats (such as box-and-whisker plots and forest plots[81]) that are commonly used in the medical literature are unlikely to be useful for trial participants who are unfamiliar with these types of diagrams, as they are unintuitive for those who have not been taught how to interpret them. Adding pictographs to numerical descriptions of incremental risk may improve understanding compared to the numeric text alone[82]. Pictographs can be effective even for people with low levels of numeracy, and were rated as being an effective, trustworthy and scientific visual format (compared to pie charts, bar charts, sparkplug

diagrams, clock diagrams and tables)[83]. Figure 1.2 gives an example of a pictograph used to convey the results of a trial run by the MRCCTU at UCL. Pie-charts can convey the gist of information, but less able to achieve accurate understanding[83], and using bar charts instead of pie charts results in better comprehension[84].

Figure 1.2: Example of a pictograph to visually convey trial results



1.9.4 Framing of information

How information is framed can affect how it is interpreted. Health information can be 'gain' framed, (focusing on what people may gain from a behaviour or treatment), or 'loss' framed (emphasising what people may lose if they do not adopt the behaviour or treatment). While the factual content of gain and loss-framed messages of the same results are equivalent, the effects they have differ. For encouraging people to adopt disease prevention approaches, a meta-analysis found that gain-framed messages are more persuasive (i.e. people are more likely to adopt the disease prevention approach) than if the message is loss-framed[85].

1.9.5 Layout and visual presentation

The layout and visual presentation of materials aimed at lay audiences can help or hinder comprehension. Guidance on the layout of documents for lay people often includes advice such as:

- Use of 12 point size and use of a clear font
- Good contrast between background and text
- Avoiding block capitals
- Left aligning text, with no right justification
- Leaving plenty of white space around the text and other content
- Use of headings and sub-headings to help readers navigate the text
- Use of bold text for emphasis rather than italics or underlining
- Avoiding clutter[86].

An RCT comparing different versions of a Patient Information Sheet (a standard one, and one with revised layout and wording following user testing) found that participants were significantly better able to find and understand information in the revised than the standard Patient Information Sheet, and nearly all preferred the revised version[87]. The layout for the revised Patient Information Sheet used a contents list on the front page, and sub-headings in large, bold text to help improve the navigability of the text. Bullet and number lists were used. The document was changed to have two columns rather than one. Colour was used to help emphasise the headings.

1.10 Importance of Patient and Public Involvement in communicating trial results to participants

The Patient and Public Involvement (PPI) literature suggests PPI in the communication of trial results to participants can be beneficial[37, 88-90], although this activity is often poorly reported[27]. The MRCT Return of Aggregate Results Guidance recommends that participant clinical trial summaries should be reviewed by patient representatives[57], and Good Participatory Practice Guidelines also recommend relevant stakeholders are consulted around how results are shared with participants[11]. PPI is likely to be important for ensuring that the participant results summary covers the items that are likely to be most important for participants, while not becoming so long that participants are put off reading it. In my own professional experience, PPI has been important for determining the most appropriate methods for communicating the results to the trial population; developing messages that are relevant and appropriate for participants; and ensuring the content is understandable and layout clear and attractive to the target audience. In some cases, patient or participant representatives have played an even more active

role in the communication of trial results, taking on the role of messenger in events, films or podcasts. One example of this that has been evaluated and published is from the PROUD HIV prevention trial[89].

1.11 Aim & scope of this PhD

This PhD aims to better understand how the results of Phase III randomised controlled trials can be communicated to participants. I explore this issue through a mixed methods study within the context of an ovarian cancer treatment trial in the UK. While a one-size-fits all approach is not likely to be appropriate across trials with very different settings, participant populations and interventions, high quality evidence is needed to inform practice. The ovarian cancer setting is interesting as the condition is serious, so the results of the trial may be 'high stakes' for participants, making appropriate communication important. It is also typical in setting to many of the cancer trials run by the MRC Clinical Trials Unit (MRCCTU) at UCL. This makes it a good setting in which to start gathering evidence to inform future practice within and beyond the MRCCTU at UCL.

This PhD explores the perspectives of both trial participants, and the staff based at trial sites (UK hospitals) who are involved in communicating trial results (including research nurses, trial coordinators and clinicians). The views and experiences of participants are obviously vital for better understanding how to share results with participants. For many trials, site staff are the bridge between the trial Sponsor and participants. The coordinating trials unit may not have contact details for participants, and communication about the trial comes via site staff. If plans to share results with participants are to succeed in this setting, communication interventions need to be both feasible and acceptable to the site staff whom Sponsors depend upon to implement them.

I have adopted a mixed methods approach for this PhD, because qualitative and quantitative approaches allow me to illuminate different facets of the issue. The quantitative study is a cluster randomised controlled 2 by 2 by 2 factorial trial within a trial, testing different approaches to communicate trial results to participants, gathering quantitative data on participant satisfaction with how the results were shared and other outcomes. This rigorous approach allows me to generate results that can identify evidence of causality between the interventions and outcomes, and to convince trialists who are used to understanding, generating and demanding this sort of evidence. The qualitative data allows me to explore the reasons why the quantitative results show what they do, and place them within the context of participants' and site staff's experience of receiving or sharing the results, aiding the interpretation of the quantitative results, and factors that may affect transferability.

1.11.1 Outline of the chapters of this thesis

1.11.1.1 Chapter 2: Quantitative Methods

This chapter presents the overarching quantitative methods used in the Show RESPECT (Show Results to Participants Engaged in Clinical Trials) study (ISRCTN96189403). This chapter relates to the overall study design, and the quantitative methods used within it, including the setting in which it took place, the PPI that informed the design and conduct of the study, the types of participants, an overview of the outcomes collected, data collection process and analysis, the randomisation process, and study management.

1.11.1.2 Chapter 3: Qualitative Methods

This chapter presents the overarching qualitative methods used in the Show RESPECT study. Show RESPECT incorporated two qualitative studies: one focusing on the perspective of patients around receiving the results of the trial they had taken part in, and the other focusing on the perspective of site staff who had been involved in sharing the trial results with participants. Both the patient and site staff qualitative studies used data collected through semi-structured interviews and free-text responses to the quantitative questionnaires on the experience of receiving or sharing trial results, completed by patients and site staff. This chapter gives an overview of qualitative methods used within Show RESPECT including sampling and data collection, data processing, the analysis process and model used to frame the analysis, discussion of my positionality and how that may have affected my research, and the triangulation approach used within Show RESPECT.

1.11.1.3 Chapter 4: Interventions tested within Show RESPECT

This chapter describes the communication interventions that were tested in Show RESPECT, including the process of selecting the interventions, their development, the process of delivering the interventions within Show RESPECT, and patient and public involvement in these aspects. Show RESPECT gathered data on a Basic Webpage, an Enhanced Webpage, a Posted Printed Summary and an Email List.

1.11.1.4 Chapter 5: Patients' perspectives on the effectiveness of the Show RESPECT interventions

This chapter relates to the patient data from Show RESPECT, including both quantitative and qualitative data. It reports results from Show RESPECT including the delivery of the interventions and the baseline characteristics of patient participants. Data that relate to the primary and secondary quantitative outcomes are then presented alongside the qualitative findings that relate to

those outcomes, using a 'following the thread' triangulation approach. This chapter concludes with a short discussion of these results, including key findings, strengths and limitations.

1.11.1.5 Chapter 6: Site staff perspectives on the benefits, feasibility and resources needed to share the ICON8 results with participants

This chapter relates to the site staff from Show RESPECT, including both quantitative and qualitative data. It reports on the baseline characteristics of site staff who took part in the study, their views on sharing results with participants generally, and their views on the processes used in Show RESPECT. It then goes on to explore the resource implications of the Show RESPECT interventions for both sites and the Clinical Trials Unit (CTU), including staff time and other costs. Quantitative and qualitative data that relate to the same topic are presented alongside each other, using a 'following the thread' triangulation approach. This chapter concludes with a short discussion of these results, including key findings, strengths and limitations.

1.11.1.6 Chapter 7: Patients' thoughts and feelings on receiving the ICON8 results

This chapter explores the qualitative data from patients and site staff around participants' thoughts and feelings on receiving trial results. It also includes quantitative data on participants' reaction to receiving the results. It starts by exploring patients' motivations for joining the trial in the first place, as this may influence their desire to receive results and their reaction to those results. It then goes on to explore their expectations around whether they would be offered the results, and whether they wanted to receive them. It then looks at whether patients understand the range of potential outcomes a trial may have, as this may affect their reaction to receiving the results. It goes on to explore patients' reaction to finding out the results, including their intellectual response and emotional response. It finally explores patient and site staff views around sharing trial results with other stakeholders, including family members of trial participants (including participants who die during trials); other patients and general practitioners. This chapter concludes with a short discussion of these results, including key findings, strengths and limitations.

1.11.1.7 Chapter 8: What aspects of the Show RESPECT interventions influenced satisfaction with how the results were shared?

This chapter explores mostly qualitative data from site staff and patients around what aspects of how the results were communicated influenced participants' satisfaction with how the results were shared, to explain the results around satisfaction reported in Chapter 5. It starts by looking at opinions on the communication medium in principle (not specific to the

interventions tested in Show RESPECT), before exploring views on the information contained within the ICON8 results summaries. It then focuses on the information products used within Show RESPECT. It goes on to look at the issue of personalisation in the context of sharing trial results, and whether results should be shared on an opt-in or opt-out basis. The chapter concludes with a short discussion of the key findings, the strengths and limitations of this study.

1.11.1.8 Chapter 9: What other factors influenced satisfaction with how the results were shared?

This chapter explores qualitative and quantitative data from patients and site staff on other factors that may have influenced patient satisfaction with how the ICON8 results were shared. These factors can be divided into factors related to the trial itself, applying to all participants (including the disease area, what the trial is comparing and its design, what the results showed) and characteristics that vary between participants within a trial (including the demographic characteristics of patients, their health and experience during the trial, their understanding of the trial, expectations around receiving results and access to support). While these factors are generally not controllable in the same way that the aspects of the mode of communication are, understanding these factors, how they interact with each other and their impact on satisfaction, may be helpful when thinking about how transferable or generalisable the Show RESPECT findings are to other studies with different trial and patient characteristics. The chapter concludes with a short discussion of the key findings, strengths and limitations of this work.

1.11.1.9 Chapter 10: Discussion and conclusion

This chapter summarises key findings from the Show RESPECT study, puts them in the context of the wider evidence base and explores their implications for future policy, practice and research. It proposes a framework to help trialists plan how to share results with participants in different trial contexts, ending with a call to action to improve how this is done.

2. Quantitative methods

2.1 Overview of scope of this chapter

This chapter presents the overarching quantitative methods used in the Show RESPECT (Show Results to Participants Engaged in Clinical Trials) study (ISRCTN96189403). Show RESPECT is a mixed methods cluster randomised 2 by 2 by 2 factorial trial, testing different approaches to sharing results with trial participants. It collected both qualitative and quantitative data from trial participants and the site staff who were involved in sharing trial results with participants. This chapter relates to the overall study design, and the quantitative methods used within it, including the setting in which it took place, the types of participants, an overview of the outcomes collected, data collection process and analysis, the randomisation process, and study management. Chapter 4 gives details of the interventions tested within Show RESPECT, and Chapter 3 describes the qualitative methods used.

2.2 Aim

The Show RESPECT study sought to generate evidence to inform trialists on how to share results with trial participants through a mixed-methods cluster randomised factorial study within the ICON8 trial. Show RESPECT tested the following three hypotheses, in terms of participant satisfaction with how the results were communicated:

1. An enhanced webpage will be superior to a basic webpage
2. A printed summary sent by post will be superior to no printed summary
3. An invitation to join an email list will be superior to no invitation to join an email list

Quantitative data was collected from patients, site staff and trials unit staff, and qualitative interviews carried out with trial participants and site staff to understand more about their experiences and views around how results are shared with trial participants.

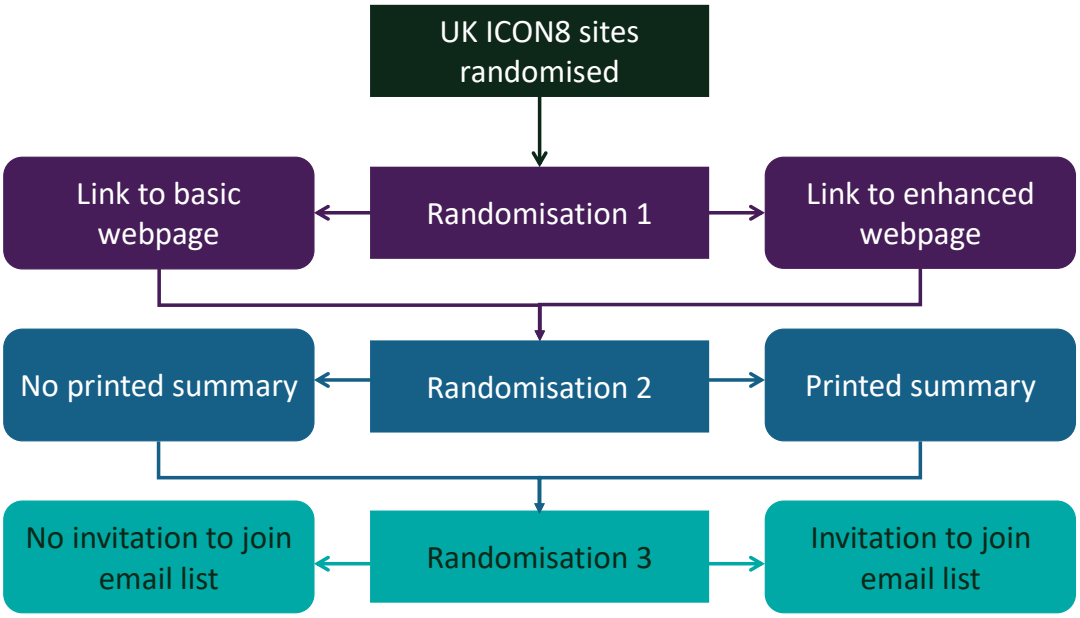
2.3 Study design

2.3.1 Show RESPECT design

Show RESPECT was a cluster randomised 2 by 2 by 2 factorial mixed methods trial embedded within the ICON8 Phase III randomised controlled trial (see Section 2.3.2 for more information on the ICON8 trial). Each ICON8 UK trial site (secondary or tertiary hospital) that agreed to take part in the Show RESPECT

study was randomised to a combination of interventions, as shown in Figure 2.1. Allocation to each intervention within a randomisation was on a 1:1 ratio.

Figure 2.1: Show RESPECT schema



Quantitative data were collected from both participants in the ICON8 trial, and site and clinical trials unit (CTU) staff who were involved in sharing the results with trial participants. Qualitative interviews were carried out with both participants in the ICON8 trial and site staff to explore their experiences and views around the sharing of trial results with participants.

2.3.1.1 Rationale for cluster design

Each ICON8 hospital taking part in Show RESPECT was a cluster for the purposes of the Show RESPECT study. A cluster design was appropriate for this study, as it was felt that implementing individual randomisation would be impractical for sites, being harder to manage than using the same approach for sharing results with all their ICON8 patients. There was concern amongst the study team that the administrative burden of individual randomisation would deter sites from agreeing to be part of the study. There was also the potential for 'cross contamination' if patients at a site are part of the same support groups and talk about how they found out the results to others. This could potentially lead to some patients being disappointed that they did not learn the results in the same way as others at that site. Using each site as a cluster simplifies delivery of the intervention for sites, and reduces the risk of cross contamination.

2.3.1.2 Rationale for factorial design

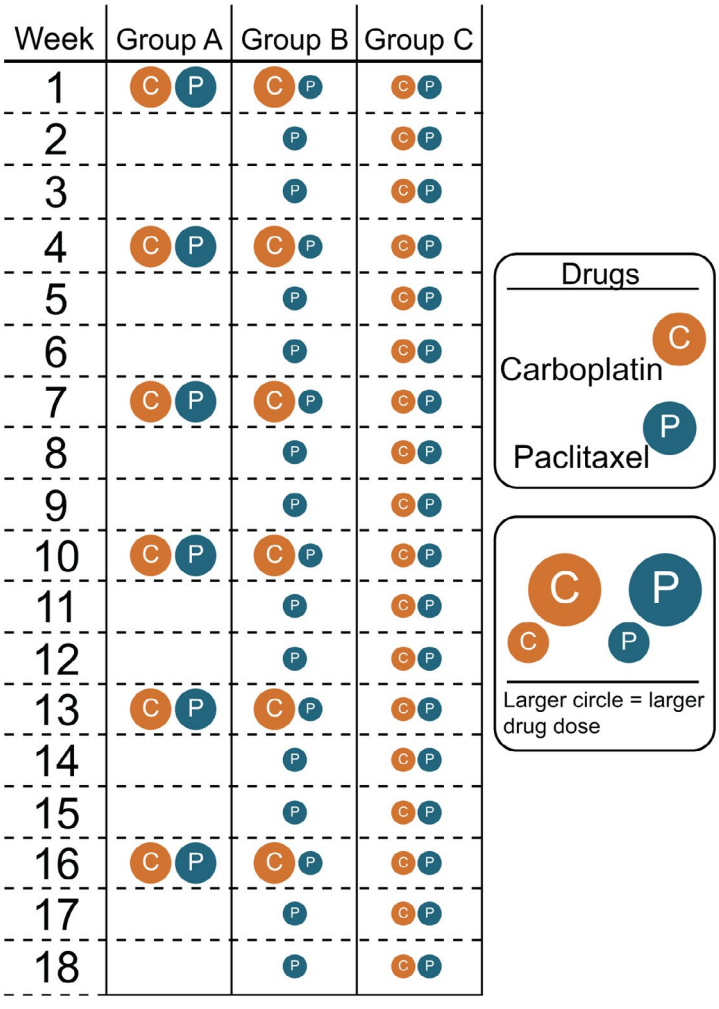
Factorial designs allow for efficient evaluation of more than one intervention in a single study[91]. As there was no reason why the interventions tested in Show RESPECT could not be used in combination, as well as separately, the 2 by 2 by 2 factorial design offers more statistical power for a given sample size than a multi-arm design testing the same number of combinations would.

My prior assumption was that there would][not be any important interactions between the interventions. Hence the primary analysis was of the main effects of each intervention adjusting for the others. However, for the primary outcome I also tested each of the three two-way interactions, and also report the effect of each of seven intervention combinations relative to control. In the event of statistically significant and qualitatively important interaction(s) I planned to change the analysis approach to report as primary analysis for the primary outcome the effect of the three (or even seven) intervention combinations relative to control, as determined by the interaction findings.

2.3.2 The ICON8 trial

The ICON8 trial is a Phase III randomised controlled trial looking at which chemotherapy schedule should be used for women with ovarian cancer (ISRCTN10356387). ICON8 compared three-weekly chemotherapy cycles (the current standard of care), to two different weekly schedules, with either both drugs being given weekly, or paclitaxel given weekly and carboplatin being given once every three weeks (Figure 2.2). 1,566 women took part in ICON8, 89% of whom were from the UK. There were also some participants from South Korea, Ireland, Mexico, Australia and

Figure 2.2: ICON8 chemotherapy schedules



New Zealand. ICON8 included patients with newly diagnosed, histologically confirmed, FIGO (1988) stage IC/IIA (high-risk histology) to IV ovarian cancer. Most participants in ICON8 had stage IIIC or IV disease, meaning the cancer had spread outside the pelvis and, in the case of stage IV, to other organs. Participants were enrolled between 2011 and 2014, meaning that, by the time Show RESPECT data were collected, all had been taking part in the trial for between 4 to 8 years. Follow-up mainly took place via face-to-face clinic visits. Results from one of the co-primary endpoints, progression-free survival, were published in 2019[92]. These results showed no evidence of difference in progression-free survival between the three arms. Participants were still in follow-up to allow collection of data on overall survival, which is the co-primary outcome. The ICON8 team were keen to share results with participants, but unsure how best to do it.

2.4 Selection of trial and sites

2.4.1 Why ICON8 was selected as the trial in which to embed Show RESPECT

ICON8 was selected as the trial in which to embed the Show RESPECT study as it was a Phase III randomised controlled trial with primary results to communicate in the planned timeframe, and many UK sites. The ICON8 trial team were keen to share results with participants, and were willing to embed a methodological study to gather data to inform how best to do this.

Ovarian cancer provides an interesting context for a study of how to communicate results to participants, as outcomes for women with ovarian cancer can vary widely, with some whose cancer responds well to treatment, while others experience disease progression and/or death soon after treatment. In the UK, five-year survival for stage III disease (which includes less severe disease than IIIC) was 27% and 13% for stage IV disease, for women diagnosed during this time period[93]. Side-effects from treatment are also common. The patient population, being predominantly older women, also raise interesting challenges around the accessibility of online information. All these factors mean there is substantial uncertainty about how to communicate trial results to this patient population, and how those results will be received by participants.

The UK sites that are part of the ICON8 trial are typical of those in cancer studies run by the MRC Clinical Trials Unit at UCL (MRCCTU): a mixture of district general and specialist hospitals all within the UK National Health Service (NHS). The MRCCTU does not have direct contact with ICON8 participants; all communication with participants goes via the sites which care for the participants, and MRCCTU holds no contact information for

participants. This is standard practice for MRCCTU cancer trials, but does raise challenges in terms of communication with participants. These factors mean the results of Show RESPECT around the feasibility of the interventions tested are likely to be generalisable to other cancer studies run by the MRCCTU at UCL.

2.4.2 Selection of ICON8 sites for Show RESPECT

All 83 ICON8 sites in the UK were invited to take part in the Show RESPECT study. Of these, 43 sites were randomised. Reasons for sites not being included in Show RESPECT were lack of eligible participants (5 sites), sites lacking capacity to support the study (6 sites), sites declining to take part (4 sites), sites expressing interest in the study but failing to obtain the necessary approvals within the study timeframe (12 sites) and sites not responding to the invitation to take part in the study (13 sites). Sites from outside of the UK were not invited to take part in Show RESPECT as they had very few ICON8 participants alive at the time the results were available, so it was not worth the work required to obtain the relevant national approvals for these countries.

2.5 Participants

There were three categories of participants in the Show RESPECT study:

1. ICON8 participants from the sites randomised within Show RESPECT (referred to as 'patients')
2. Staff from participating sites who were involved in sharing the results with participants (referred to as 'site staff') - this includes research nurses, trial coordinators and administrators, and clinicians
3. Staff at the MRC Clinical Trials Unit at UCL who were involved in sharing the results with participants (through developing and implementing the interventions)

2.5.1 Eligibility criteria

To be eligible for Show RESPECT, patients had to meet the following inclusion criteria:

- Participant in the ICON8 trial
- Currently being followed up at an ICON8 trial site that was participating in Show RESPECT
- Aged 18 years or older

Patients were excluded if they met any of the following exclusion criteria:

- Participant had previously informed their site that they do not wish to attend any further visits in relation to the ICON8 trial, or provide any further

data (sometimes referred to as 'withdrawal of consent'); participants who previously stopped ICON8 trial treatment earlier than expected but continue in ICON8 follow-up were not excluded, nor were participants who have reduced follow-up arrangements but still contribute data to the ICON8 trial.

- Lost to follow-up from the ICON8 trial
- Site staff consider the patient to be too unwell to be contacted about this study

Site staff were eligible if they worked at a Show RESPECT site and were involved in sharing the ICON8 results with participants, or responding to queries about the results from patients.

2.5.2 Consent

No informed consent was required for the study interventions, as we would expect trial results to be shared with participants regardless of this study. Randomisation was site level (each site being a cluster), rather than individual, so individuals did not have the opportunity to opt out of randomisation. In addition, most of the interventions offered are by nature opt-in, i.e. trial participants could choose whether or not to visit a webpage, or join an email list.

We provided participants, site and CTU staff who were sent quantitative questionnaires with information about why we are collecting the study data. This information was integrated into the data collection tool and included explanations of:

- What the data collected will be used for
- How data will be stored
- Confirmation that provision of data for the study is entirely voluntary

Participants in Show RESPECT are not placed at any significant risk through being randomised to receive information about ICON8 trial results in different ways, and there is no strong evidence to recommend one approach above others. In order to avoid overloading participants with information (and likely reducing the completion rate as a result) we therefore kept participant information short and focused on key information only.

In line with the HRA's guidance on proportionate approaches to informed consent for self-administered questionnaire-based research, we did not ask for a signature to confirm participants have read and understood the information; instead, completion and return of the questionnaire were taken to indicate consent to use the data had been given.

2.6 Overview of outcomes

2.6.1 Patient and public involvement in selection of the quantitative outcome measures

I carried out a PPI survey of 76 patients to inform the design of the Show RESPECT study. I asked respondents which aspect was most important to consider in how we measure the success of sharing trial results with participants (with options identified from the literature review). The three most popular options were:

- Can participants understand the results? (37% of respondents)
- Does it tell people everything they want to know about the results (35% of respondents)
- How satisfied participants are with how the results were communicated to them (15% of respondents)

The other options (how many people choose that approach, would they be willing to take part in future research, would they recommend taking part in a trial to friends/family, will people who want to know the results actually be told them, and how long it takes for participants to be told, after results are known to researchers) were only chosen by a handful of respondents (1-3 each). In the free text comments, many commented that there was no point communicating results if participants could not understand them (and many had experience of information about trials being communicated in a way they could not understand). Those who selected satisfaction pointed out that this outcome will incorporate both understanding and whether it told people what they wanted to know.

Upon consideration, the Show RESPECT team felt that satisfaction would be a better primary outcome for the study as it would, in theory, capture participants' views across whichever aspects of receiving the results were important to them personally. We felt that a person would be unlikely to report being satisfied if the results had not been understandable, or had not told them what they wanted to know. Conversely, it would be possible for someone to find the results understandable, but be very unhappy about receiving them, which would not be a good result.

I wanted to make sure that the way in which we asked about our proposed primary outcome (satisfaction with how the results were communicated) would be clear and understandable to patients, and capture the concept we were interested in. I asked attendees at a PPI discussion group for participants in ovarian cancer trials to imagine they were participants in the ICON8 trial, and had received the printed summary of results through the post. They were asked

to read through the ICON8 results summary. I then gave them one of three options for primary outcome text:

A. “How satisfied are you with how we shared ICON8 results with you?”
B. “How satisfied are you with how you heard about the results of ICON8?”
C. “How satisfied are you with the way you found out the results of ICON8 (rather than the results themselves)?”

All questions asked people to ‘Circle the best answer’ and gave five possible answers on a scale:

- Very unsatisfied
- Quite unsatisfied
- Neither satisfied nor unsatisfied
- Quite satisfied
- Very satisfied

I then asked participants why they selected the option they had. The purpose of this was firstly to see if participants were answering the question I thought I had asked (or if we would get comments back on what the results showed), and also to help me understand more about what is likely to influence satisfaction with how the results were shared. None of the proposed questions elicited responses to do with satisfaction about the results themselves. Attendees favoured option C as the clearest. Option B produced some ‘incorrect’ conclusions and seemed to lead people away from talking about how the results had been shared with them. Women who took part in the discussion group were very supportive of both the proposed study in general, and the use of satisfaction as the primary outcome measure. Based on this, I chose option C as the wording of my primary outcome measure.

Once the patient feedback questionnaire was drafted, I asked the patient representative on the Show RESPECT Study Steering Group to review it and provide feedback about clarity.

2.6.2 Primary outcome

The primary outcome for Show RESPECT was patients’ satisfaction with the way in which they found out the results. The final wording for the outcome measure was “How satisfied are you with the way you found out the results of ICON8 (rather than the results themselves)?”. This was measured using a Likert-type scale from (1=Very unsatisfied, 2=Somewhat unsatisfied; 3=neither satisfied nor unsatisfied; 4=Somewhat satisfied; 5=Very satisfied).

All the outcomes collected from site and CTU staff are considered secondary outcomes. However, amongst the outcomes collected from site staff, we

consider cost to site per patient as the 'primary' outcome. This is a composite endpoint that is made up of:

- an estimate of the cost of the time taken to deliver the interventions at a site
- an estimate of the cost of the time taken to deal with queries
- The cost of any non-staff costs incurred by sites

These total costs were divided by the number of eligible ICON8 patients at the site (to whom the PUIS was sent).

2.6.3 Secondary outcomes

The secondary outcomes assessed in Show RESPECT can be split into the following categories:

- Effectiveness and process outcomes, collected from patients:
  * Did the information about the trial results tell patients everything they wanted to know?
  * How easy did patients find it to understand the results?
  * How easy did patients find it to find out the results?
  * How upsetting did patients find the results?
  * How willing are patients to take part in research again in the future?
  * How likely are patients to recommend taking part in research to friends or family?
  * Are patients glad they found out the results?
  * Do patients regret finding out the results?
  * What proportion of patients used the intervention(s) offered?
  * What proportion of patients who wanted to find out the results reported finding out the results?
  * What proportion of participants who did not want to find out the results who reported finding out?
  * Would participants prefer to have been given the opportunity to find out the results in a different way?
  * If they found out the results in several ways, which did they prefer?
- Process outcomes, collected from site staff
  * What costs were incurred by sites to communicate results to participants, per patient?
  * How much time was taken to deliver the interventions?
  * Who delivered the interventions?
  * What challenges did sites face implementing the interventions?
  * How many queries did sites receive from patients following the results being communicated?
  * How long did it take to deal with a single enquiry, on average?

    * What non-staff costs were incurred by sites?
    * What proportion of patients did the Patient Update Information Sheet go out to?
    * What proportion of patients in sites randomised to the Printed Summary were sent the Printed Summary?
    * How many patients opted out of receiving the Printed Summary?
- Other outcomes, collected from site staff, including preferences and concerns
    * What method of communicating the results to participants did site staff prefer?
    * What concerns did site staff have with the interventions / process of communicating results?
    * Do site staff think the intervention(s) they were randomised to should become standard practice for the trials they are involved in?
    * Would site staff prefer to have given participants a different way to find out the results? If so, how and why?
    * What would site staff like to do differently for the next trial they are involved in communicating results for?
- Process outcomes, collected from CTU staff
    * How much time did it take CTU staff to develop and deliver the interventions?
    * How much did each intervention cost the CTU?

Outcomes included a range of question types, including Likert-type scales, single and multiple-choice questions, free text and numerical response questions. See Section 2.10 for more detail on the data collection process and instruments.

2.7 Randomisation

Sites were randomised in blocks of 8 (the number of allocation arms) after they had obtained the necessary approvals. This was phased as sites took different lengths of time to obtain approvals. Randomisations were conducted at five distinct time points, with the number of sites included at each phase as follows:

1. 8 small and 8 medium sites (one block of each size)
2. 8 large sites (one block)
3. 4 small and 4 medium sites (randomised jointly as a ‘mixed’ block)
4. 3 small, 1 medium and 4 large (randomised jointly as a ‘mixed’ block)
5. 2 small and 1 large (randomised jointly, an ‘incomplete block’ of final trial sites)

Randomisation was conducted through random permutation within blocks. For the incomplete block at the final phase, the allocations were the first three of the eight possible allocations after permutation.

To ensure allocation blinding, the Show RESPECT statistician generated the allocations for the blocks (i.e. randomly ordered the 8 possible allocation arms for each block) and was aware of which clinics featured in each block, while a second statistician, unaware of these allocations, randomly permuted the clinic names within blocks. I then matched the allocations and clinic names for each block, and, once confirmed by both statisticians that this had been done correctly, revealed the allocations to the trial team. Sites were then informed of their randomised allocation and sent the matching Patient Update Information Sheet.

2.8 Blinding

Once randomisation had been performed, it was not possible to blind site staff to their site's allocation. ICON8 patients were not informed that the way they were being offered the results was determined by randomisation and were not aware of the interventions being offered to patients at other sites.

2.9 Sample size

At trial sites, the allocated Show RESPECT intervention was offered to all eligible ICON8 participants (through the Patient Update Information Sheet). However, not all eligible participants were approached for data collection, so as to reduce the burden on participants and staff. In cluster randomised trials, the marginal information value of each participant declines as cluster size increases[94]. Specifically, at small sites (≤5 eligible participants), all eligible participants were invited to provide outcome data, but at medium sites (6-12) we aimed to collect outcome data from 6 participants and from large sites (≥13) we aimed to collect data from 12. For medium and large sites, the individuals invited to participate were selected at random centrally. At medium and large sites, if a participant who was invited to take part chose not to, the next participant from a randomly ordered, centrally held list was invited to take part to replace the original participant, until the target number of participants at that site was reached, or no eligible participants remained.

The primary outcome measure was ordinal but for simplicity, because of lack of knowledge of its likely distribution, and to be scientifically conservative, I considered it as a binary outcome for our power calculations. I anticipated that the proportion of respondents "satisfied" without any of the research interventions would be between 20 and 80%, and in the absence of specific

prior information considered values of the Intracluster Correlation Coefficient (ICC) between 0.01 and 0.05. I considered power to detect an effect for any of the three interventions, for simplicity considering each in turn, i.e., effectively conducting a power calculation for each intervention assuming the other two would have no effect. I also assumed no appreciable interactions between the three interventions. Based on 21 sites with and without an intervention, and an average of 4 respondents per site (172 in total), at an ICC of 0.01 the study would have 80% power to detect an increase from 20 to 40%, from 50 to 71%, or from 80 to 95% in the satisfied group. Should the ICC have been 0.05 then this sample size would have provided 80% power to detect an increase from 20 to 42%, 50 to 73%, or 80 to 95%. No power calculations were made for the secondary outcomes.

2.10 Data collection

Quantitative data were collected from patients, site staff and CTU staff using self-completed case report forms (questionnaires). Table 2.1 summarises the method and timing of data collection from each of these three groups. Sites kept logs to record each step of the data collection process. These were regularly collected for monitoring purposes by the Show RESPECT data manager.

All quantitative participant-level data collection specific to Show RESPECT were collected on a single questionnaire. The questionnaire was sent by site staff to participants by post, together with a stamped addressed envelope for participants to return their completed forms to the MRCCTU at UCL. Sites were sent the questionnaires pre-populated with the trial ID numbers of relevant participants (i.e. those who were randomly selected to provide data at their site). Prior to sending these questionnaires out to the selected participants, sites were asked to confirm that the participant is still alive. This was done through site staff contacting each selected participant's GP to check the patient has not died. The questionnaire was sent within a week of this check. This check could be omitted if the site had had contact with the participant within the preceding two weeks (e.g. for a clinic visit), and had no reason to believe the participant was too unwell to receive the questionnaire. In cases of doubt, the GP was contacted to check the patient was alive.

Sites were asked to follow-up with participants who have not returned their forms within a month of the questionnaire being sent, to encourage them to return them. Before contacting patients, sites were asked to confirm the participant is still alive through the same process as described above. To boost data collection rates, an incentive (£15) was offered to sites for each completed

Table 2.1: Method and timing of quantitative data collection

Data collection type	Method	Timing
Quantitative data from ICON8 trial participants	Single questionnaire, distributed by site staff, with site-level incentives to increase response rates	Began at each site 1 month after administration of last intervention (Patient Update Information Sheet sent/ email sent / printed summary sent, depending on randomisation of site) to the last patient at that site. Sites were reminded of when this was.
Quantitative data from ICON8 site staff	Case Report Forms for site staff to complete; one immediately after intervention delivery, one later (more than one set per site allowed, if several people were involved in the process of communicating results)	Data about the process of communicating results was collected immediately after interventions have been delivered. Data about the response from patients was collected 2-3 months after administration of last intervention.
Quantitative data from MRCCTU trial staff	Case Report Forms for CTU staff to complete; one immediately after intervention delivery, one later (one set per team member involved in dissemination of trial results)	Data about the process of communicating results was collected immediately after interventions have been delivered. Data about the response from patients and sites was collected 2-3 months after administration of last intervention.

questionnaire returned to the MRCCTU. If a pre-selected participant chose not to complete the questionnaire, or became ineligible for the study, the site was asked to contact an additional participant as a substitute, if there were other ICON8 participants at the site who were not selected in the initial Show RESPECT sample. A list of up to 6 (for medium recruiting sites) or 12 (for high recruiting sites) substitutes, selected at random (or, where it equals all the eligible participants at a site, ordered at random) was prepared in advance by the trial statistician, but was not revealed to sites until required (i.e. participant had confirmed to site that they did not wish to complete the questionnaire, or a completed questionnaire had not been returned to the MRCCTU at UCL despite the site having reminded the participant three times). Substitute participant numbers were revealed to sites one at a time, to prevent selection bias.

Sites were provided with a specific log to record each stage of this process for each participant, i.e. the date the Patient Update Information Sheet was distributed, the date postal interventions were distributed (if applicable to their site), the date the patient's GP was contacted to confirm the patient has not died, the date the CRFs were distributed and dates of any further attempts to contact participants to encourage return of CRFs. These data were used for central monitoring processes.

Some data from the ICON8 trial was used in Show RESPECT (year of birth and ICON8 trial arm). The ICON8 trial ID number was used to link these data with the Show RESPECT questionnaire data.

2.10.1 Processing the data

Case Report Forms and patient questionnaires were returned to the MRCCTU at UCL by post. Upon arrival, I logged the forms, and systematically checked for any issues of concern (e.g. participants finding ICON8 results extremely upsetting, or issues of potential harm where we might have a duty of care to act, such as participant reports of suicidal thoughts). Any issues found were passed in the first instance to the Clinical Reviewer and discussed, involving the ICON8 team where appropriate. If it was considered necessary by the Clinical Reviewer, we informed the site staff of any concerns so that they could take appropriate action. Forms were then passed to the Show RESPECT Data Manager for data entry onto the study database.

2.10.2 Quality Assurance

To ensure the primary and secondary outcomes were correctly entered on the database, I checked 50 patient questionnaires and 50 forms from site and CTU staff on the database against the original form. Data entry accuracy was 100% for the patient questionnaires, and 99.55% for the site and CTU staff forms checked. Once data checking was complete, the database was locked and data extracted from the study database for analysis.

The Show RESPECT team kept logs to ensure that all the necessary activities were happening at the right time, and collected logs from sites for monitoring purposes. With the Show RESPECT Data Manager, I prepared monthly monitoring reports that covered:

- Distribution of Patient Update Information Sheets
- Distribution of Participant Summaries
- Intervention uptake based on link clicks and logs from sites
- Eligibility checking prior to distribution of the patient questionnaire
- Return of patient questionnaires
- Return of site staff questionnaires

- Return of CTU staff questionnaires
- Site opening and randomisation status
- Site closure

These reports were discussed at the monthly Study Management Group meetings, and action decided to address any issues that had been identified (such as low rates of questionnaire returns from particular sites).

2.11 Analysis

2.11.1 Patient data

The Show RESPECT Statistical Analysis Plan for patient data was written by the study Statistician (Professor Andrew Copas), with input from me. The Statistical Analysis Plan was finalised and signed off prior to database lock. I carried out the analysis under the supervision of Professor Copas. The analysis of the primary outcome measure was independently (double) programmed by another statistician. Statistical analysis was carried out in Stata version 15.1 and 16.1 (Stata Corp, Texas).

The primary outcome measure was defined only for participants who received the ICON8 trial results, and hence analysis for this outcome was restricted to participants who reported receiving the ICON8 results. For this reason, I describe the primary analysis as following modified intention to treat (mITT). All other secondary outcomes are similarly only defined for participants who received the ICON8 results, with the exception of 'report finding out the ICON8 results', which I present separately among participants who report they wanted to find the results out, and among participants who report they did not. To assess the overall effect of the intervention, it is important to interpret the results of the primary outcome alongside results concerning the possible effect of the interventions on whether participants actually found out the ICON8 results.

In the ICON8 setting, patients' health may be poor and may deteriorate before the Show RESPECT interventions were received or between intervention exposure and follow-up by questionnaire. Patients who died or became too sick to complete a questionnaire were not considered 'eligible' for data collection or analysis, and were not considered as missing data.

The prior assumption in the Show RESPECT trial design is that there will not be any important interactions between the three interventions. Hence, the primary analysis was of the main effects of each intervention adjusting for the others. However, for the primary outcome measure I also tested each of the three two-way interactions, and report the effect of each of seven

intervention combinations relative to control. Adjustments were not made for multiple testing, so all confidence intervals presented are at the standard 5% significance level.

To reflect the trial design, I adjusted for site size stratum, and also early (first two phases) vs. later randomisation phases. All models included random effects for site. Estimates were also adjusted for age (continuous – linear), education (graduate vs. not), and internet use (daily vs. less).

Effect measures for the interventions are estimated and presented based on regression models. Ordinal random effects logistic regression was used for the primary and other Likert scale outcomes unless the proportional odds assumption was clearly violated. The response categories were merged for the regression analysis in the event of very low reporting of one or more categories (<5% of responses). All decisions about merging response categories were taken based on an initial dataset without cluster or allocation identifiers.

For the primary outcome measure only, I conducted pre-specified subgroup analyses by age group (≤70 vs. >70), allocated arm of the ICON8 trial, education category (graduate vs. not), and reported internet use (daily vs. not). For each subgroup analysis the effect of each intervention within subgroups were presented and an interaction test was conducted. All interactions were binary subgroups, except for age which was used as a continuous variable. These subgroup analyses were conducted for each of the three interventions 'by margin'.

2.11.2 Site and CTU staff data

The Statistical Analysis Plan for the site staff and CTU data was written by me, with input from Professor Andrew Copas. I used an intention to treat approach for this analysis. All staff were analysed according to the interventions their site was allocated to, regardless of whether they were personally involved in the administration of a particular intervention. To reflect the design, I adjusted my analysis for clinic size stratum. I did not adjust for early vs late randomisation phases (which I did for the patient data), as the small number of responses we have limits our ability to adjust for different factors, and I suspect randomisation phase is less likely to influence site staff outcomes than clinic size stratum. I conducted an available case analysis, and did not impute missing data, as there was nothing to inform the imputation.

I estimated and present effect measures for the interventions based on regression models. Most of the quantitative outcomes are categorical (mostly either ordinal or binary). I used ordinal logistic regression for ordinal outcomes. Binary outcomes were analysed using binary logistic regression. All models

included random effects for site. Unordered categorical outcomes (e.g. preferred approach for sharing results) were summarised using descriptive statistics, with tests conducted for each intervention using a clustered data version of a chi-squared test. I used linear regression to analyse the costs of the different interventions, adjusted by strata. For continuous outcomes I used mean differences to summarise the effects.

Secondary outcomes were not double-programmed. I was not blinded to allocation. However I conducted some preliminary analysis tasks using a dataset in which individual and cluster identifiers, and allocation identifiers, had been removed, including consistency checks and decision making to inform the model.

For continuous variables, I looked at the distribution to assess model fit, and decided whether the data needed to be transformed (if distribution was clearly skewed). For ordinal outcomes I merged response categories for the regression analysis in the event of very low reporting of one or more categories (<5% of responses). Where this occurred, the lowest response category was merged with the adjacent category that had the lowest response, and the process repeated until all remaining categories had >5% of responses.

For ordinal outcomes the key aspect of model fit I needed to address is the assumption of proportional odds that underlies the ordinal logistic regression analysis I intended to apply. I based my assessment of whether ordinal regression is appropriate by inspecting the proportion of participants reporting each of the ordered response categories for each intervention in turn 'by margin'. The key deviation from proportional odds I looked for was that an intervention affects the outcome by increasing reporting at both extremes – e.g. very short time taken to deliver interventions, and very long.

No sensitivity analyses or subgroup analyses were performed on the site staff or CTU staff data, as the dataset was too small for this to be informative.

2.12 Study management

2.12.1 Study Management Group

Day-to-day management of the Show RESPECT study was carried out by the Study Management Group, which was made up of the following roles:

- Chief Investigator (me)
- Trial Manager
- Data Manager
- Trial Statistician
- Trial Clinicians

The Study Management Group met monthly to discuss any issues arising in the monitoring reports, and other aspects of study management.

2.12.2 Study Steering Group

The Study Steering Group provided oversight of the project. The Study Steering Group was made up of external experts in this area, representatives from the ICON8 trial, a patient representative, and members of the Study Management Group. The Study Steering Group met 8 times over the course of the study, and provided advice on the design, conduct and dissemination of the study.

2.12.3 Patient and public involvement in the running of the trial

A patient representative sat on the Study Steering Group. The patient representative for Show RESPECT was also a patient representative on the ICON8 Trial Management Group, so knew the ICON8 trial and its results well. She participated in steering group meetings, and sent written feedback on draft documents.

I also consulted her a number of times by telephone or email on specific issues that arose in between steering group meetings. For example, during the early part of data collection, we noted that some of the questionnaires had solicited seemingly contradictory answers relating to the primary outcome (e.g. the patient ticked 'very unsatisfied', but put in free text comments about being very satisfied). I discussed this with the patient representative, and, following that discussion, added smiley and frowny faces to the questionnaire above the relevant tick boxes to make it easier for people to distinguish, at a glance, between very satisfied and very unsatisfied. This seemed to resolve the problem.

Once the initial analysis had been carried out, the results were discussed at a Study Steering Group meeting, which included a patient representative. I also held an online discussion group with women participating in ovarian cancer trials, to ask their feedback on the trial results, how they should be interpreted, and what recommendations we should make based on them. Contributors to the discussion group were not surprised by the results. They provided input to the recommendations that we developed based on the trial results (see Discussion), and said they felt these recommendations should be strong. They also provided input on how we should share the Show RESPECT results with patients, including through patient group newsletters.

The patient representative on the Study Steering Group commented on drafts of the paper, and the summary of Show RESPECT results that we developed to

go out to ICON8 participants. She also contributed to a podcast I developed to explore the issue of sharing results with trial participants.

2.13 Ethics and approvals

The study obtained ethics approval from the London-Chelsea Research Ethics Committee, MREC number 18/LO/1011.

In addition, the Research and Design department of each participating site gave approval for the site to take part in the study. The National Institute of Health Research Clinical Research Network adopted Show RESPECT as part of its portfolio, which enabled sites to obtain payments for each ICON8 patient they recruited to Show RESPECT.

3. Qualitative methods

3.1 Overview of scope of this chapter

This chapter presents the overarching qualitative methods used in the Show RESPECT study. Show RESPECT incorporated two qualitative studies: one focusing on the perspective of patients around receiving the results of the trial they had taken part in, and the other focusing on the perspective of site staff who had been involved in sharing the trial results with participants. Both the patient and site staff qualitative studies used data collected through semi-structured interviews and free-text responses to the quantitative questionnaires on the experience of receiving or sharing trial results, completed by patients and site staff.

Chapter 4 contains a description of the interventions used within Show RESPECT to share results with participants, and Section 2.3.2 describes the ovarian cancer trial within which Show RESPECT took place. This chapter gives an overview of qualitative methods used within Show RESPECT, the patient and public involvement that informed the studies, an overview of sampling and data collection, data processing, analysis process and model used to frame the analysis, discussion of my positionality and how that may have affected my research, and the triangulation approach used within Show RESPECT.

3.2 Mixed methods approach within Show RESPECT

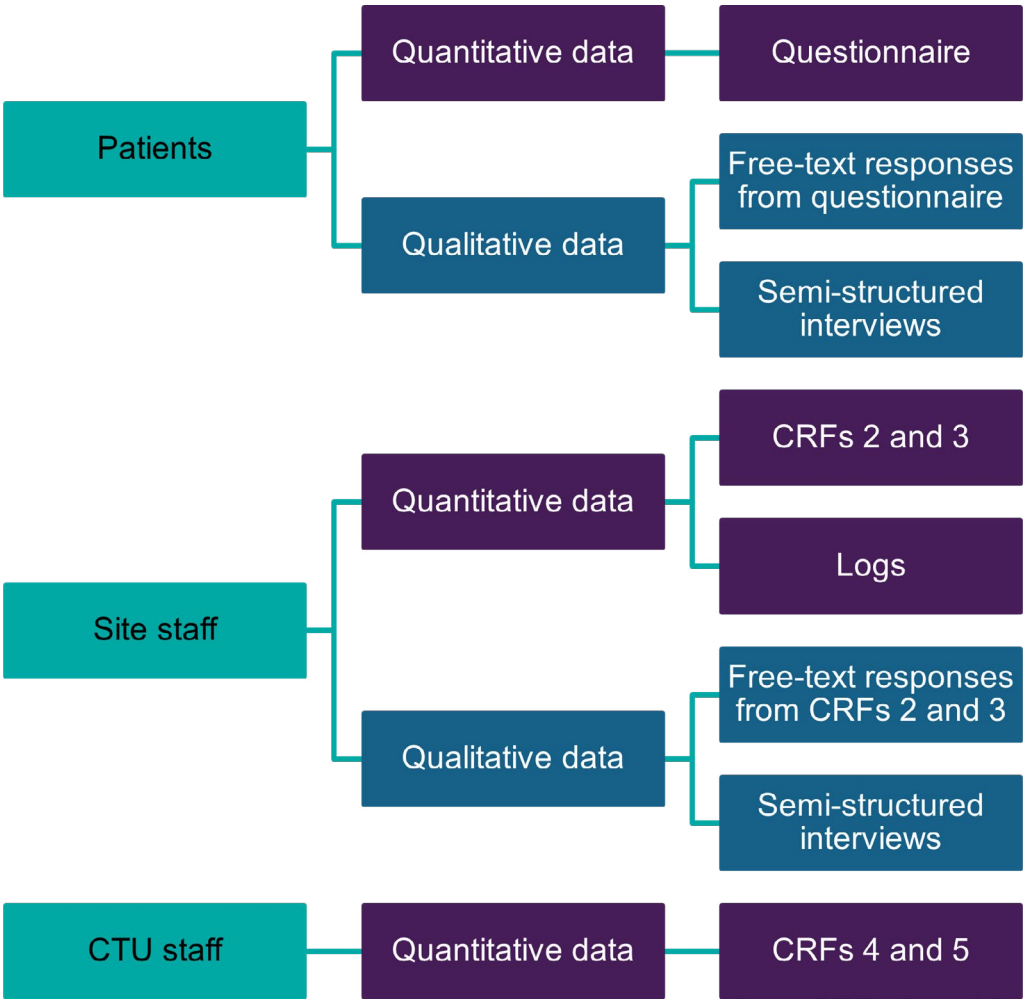
3.2.1 Role of qualitative and quantitative approaches within Show RESPECT

The aim of this research was to generate findings that could guide the practice of sharing results with participants in future trials, beyond the specific trial in which the research took place. A concurrent mixed methods design was used[95]. Figure 3.1 shows an overview of the different components of Show RESPECT.

The role of the qualitative research within Show RESPECT was threefold:

1. To explore the context in which the quantitative results were observed, describing the experience of patients and site staff around receiving/sharing the ICON8 results, within the broader context of their involvement in the trial, their previous experience and wider context
2. To provide explanation for the quantitative results, exploring the factors that influence satisfaction, motivation to receive or share results, and barriers that may make sharing or receiving results challenging

Figure 3.1: Overview of the different components of Show RESPECT



3. To evaluate acceptability and feasibility of the interventions and process used within the Show RESPECT study, particularly from the site staff perspective, to identify areas for potential improvement in future attempts to share results

The aim of the quantitative research was:

1. To evaluate the effectiveness of the interventions on ordinal outcomes including satisfaction, understanding, providing the information patients wanted to know, and ease of finding out the results
2. To identify the resources required to implement the interventions at site and CTU level

3.2.2 Qualitative research questions for patient study

Semi-structured interviews and free-text comments in feedback questionnaires were analysed to explore:

1. What are the experiences and views of women in the ICON8 ovarian cancer trial on how the results were communicated to them? (Chapter 5 and Chapter 7)

2. What aspects of the mode of communication influence satisfaction with how the results are communicated, and why? (Chapter 8)
3. What other factors influence how satisfied women in the ICON8 trial were with how the results were communicated to them? (Chapter 9)

3.2.3 Qualitative research questions for site staff study

Semi-structured interviews and free-text comments in feedback questionnaires were analysed to explore:

1. What are the experiences and views of site staff in communicating the results of the ICON8 trial to the trial participants using the approaches tested in the Show RESPECT study? (Chapter 6, Chapter 7 and Chapter 8)
2. Which approaches to communicating the results of the ICON8 trial to participants are acceptable and feasible to implement for site staff and why? (Chapter 6)

3.2.4 Sequencing of qualitative and quantitative research

Data collection for the quantitative and qualitative components of Show RESPECT was concurrent. I identified patients for the semi-structured interviews from their questionnaire responses and contact form returned alongside the questionnaire, so interviews took place after quantitative data collection for those individuals (while quantitative data collection continued for others). Interviews with site staff took place after they had shared results with participants, by which time they were scheduled to have completed Case Report Forms (CRF) 2 and 3, although this was not part of the process of identifying interviewees. As sites were randomised at different time points, implementation of the interventions was completed at some sites before others had started. Later interviews allowed me to follow-up on issues raised in the earlier interviews.

3.2.5 Triangulation of the different components of Show RESPECT

Show RESPECT used methodological triangulation, utilising qualitative and quantitative research methods and data collection techniques to throw light on different aspects of the issue being studied. I considered them to have equal weight in their contribution to addressing the research aims. I integrated the findings at the analysis stage using a 'Following the thread' approach[96]. I analysed each data set initially using approaches applicable to the type of data to identify key themes and questions. I then interrogated the qualitative data to explore issues raised in the quantitative data. I also explored issues raised in the patient data (qualitative and quantitative) in the site staff data, and vice versa. This approach was chosen as it allowed each data set to be analysed

using the techniques appropriate to the data, before being examined to see how it related to what the other data set revealed. It does not require having to translate qualitative data into a more quantitative form to allow assessment of convergence, as is required in the Triangulation Protocol approach[97].

Analysis of the qualitative data from site staff and patients was conducted within the same Atlas.ti project, using a coding scheme that developed through the concurrent analysis of the two related datasets, based on the same model (see Section 3.9). This allowed me to make comparisons between the site staff and patient data on issues of interest. I analysed the two forms of qualitative data (semi-structured interview transcripts and free-text questionnaire responses) within the same Atlas.ti project, using the same coding scheme. Atlas.ti is a computer assisted qualitative data analysis computer software package.

3.3 Qualitative approach and research paradigm

The qualitative studies used data collected by semi-structured interviews and free-text questionnaire responses, analysed thematically. I worked within the critical realist research paradigm, taking the ontological position that an external reality exists that is independent of our beliefs and understanding, but that our knowledge of that external reality is influenced by our historical, social and cultural situation[98]. The Critical Realism paradigm has an 'ecumenical' approach to data collection[99], which fits well with my mixed methods approach. Both inductive and deductive approaches are used in Critical Realist analysis. The Critical Realist paradigm means that, when interpreting my data, I must remember, when attempting to describe or explain external reality, my data and analysis is inevitably influenced by the context in which it my research took place.

Clinical trials operate within a largely post-positivist tradition, producing knowledge about the world through testing hypotheses to understand external reality, and trying to minimise researcher 'bias'. Qualitative research often emphasises the importance of interpretation alongside observation and seeks to be reflexive about how the background and context of the researcher influences the data they collect and their analysis of it, rather than try to eliminate this 'bias'. Through the process of the interviews I carried out, I could see how the participants and I were constructing knowledge during the interviews, with the process of being asked questions and reflecting on their experiences leading participants to new understanding or viewpoints.

3.4 Sampling

I used a purposive approach for sampling both patients and site staff for the semi-structured interviews, to allow me to collect data from participants with a range of characteristics that may be related to their experiences and views on sharing results. For participants, this included age, education level and frequency of use of the internet, while for site staff this included role, number of ICON8 patients at the hospital at which they work, and, for both groups, which interventions their hospital had been randomised to.

3.4.1 Sampling study sites

Initially, I identified 8 Show RESPECT sites from the first two randomisation phases from which to invite participants to take part in the qualitative studies. These sites were selected because they were feasible for the me to travel to, given the time and resource constraints of this study, as I hoped to conduct the interviews face-to-face. These eight sites consisted of one from the small stratum (which had fewer than 6 ICON8 patients), three from the medium stratum (6-12 ICON8 patients), and four from the large stratum (more than 12 ICON8 patients), covering 7/8 of the possible combinations of interventions. Patients were asked to complete a contact details form if they wanted to find out more about the interviews and return it alongside their questionnaire.

3.4.2 Sampling participants

I hoped to recruit at least two patients from each site. I also invited site staff from these sites to be interviewed. However, it soon became clear that fewer patients than I hoped were returning the contact details form to learn more about the qualitative study, and that I would be unable to recruit enough patients from those eight sites. I therefore decided to expand the invitations to sites where it was not feasible to travel, conducting interviews by telephone. As, by this stage, most of the sites had already sent out the questionnaire, I was restricted to the 11 sites from the last two randomisation phases, of which six sites agreed to help me recruit qualitative participants.

Among those patients who returned the contact details form, purposive sampling was carried out, based on their questionnaire responses, to include people offered the range of Show RESPECT interventions, different levels of satisfaction with how the results were communicated, education level, internet usage and age. Respondents who completed the contact details form and filled one or more gaps in the sampling frame were contacted with more information about the study and, if they were willing to take part, a time and date was arranged for the interview. Interviews were carried out until all the gaps in the sampling frame were filled, or until no more volunteers were

available who would fill a gap in the sampling frame. In practice, nearly all respondents who returned the contact details form and were contactable were contacted to take part, as most filled one or more gaps in the sampling frame. Table 3.1 shows the sampling frame for patients.

Table 3.1: Sampling frame for patients

Characteristic	Target
Show RESPECT randomisation	
Basic webpage	6
Enhanced webpage	6
Printed summary	6
No printed summary	6
Email list	6
No email list	6
Reported satisfaction with how the results were communicated	
Very unsatisfied to neither satistfied nor unsatisfied	n/a
Quite satisfied or very satisfied	n/a
Level of education	
No qualifications – A level	n/a
Degree / postgrad	n/a
Internet/email use	
Never	n/a
<once a week	n/a
>once a week	n/a
ICON8 arm	
A (3-weekly chemotherapy)	n/a
B or C (weekly chemotherapy)	n/a
Age group	
<50	n/a
51-60	n/a
61-70	n/a
71+	n/a
Uptake of interventions	
Basic webpage	2
Enhanced webpage	2
Printed summary	2
Email list	2
Opted out of printed summary	1

For site staff, my sampling frame included staff role, site strata, and whether or not their site had been randomised to send posted printed summaries (Table 3.2). I purposively selected site staff from the sites that were part of the qualitative study that covered these characteristics, and was able to recruit

my target number of participants for each section of the sampling frame. Invitations were sent by email.

Table 3.2: Sampling frame for site staff

Characteristic	Target
Site randomisation	
Sent printed summaries	6
No printed summaries	6
Site strata	
Small	2
Medium	2
Large	2
Job role	
Research nurse	3
Admin / trial coordinator/ data manager	3
Clinician	2

Information Power is a concept that can guide decisions around sample sizes for qualitative studies[100]. Applying the Information Power model to my study: my aim was reasonably narrow, focusing on just one aspect of trial experience (receiving results), although interviews did explore several approaches to results communication. The sample specificity was dense, with all interviewees having highly relevant experiences. As described in the analysis section below, concepts from an established model for understanding the process of information seeking and communication were applied during the analysis to guide the development of the coding frame. The quality of dialogue in most interviews was good, resulting in a rich dataset. The analysis strategy was cross-case. Taken together, these factors suggest that a moderate sample size should provide sufficient information power to meet the aims of the study.

See Section 2.9 for details of the sampling approach used for the questionnaires.

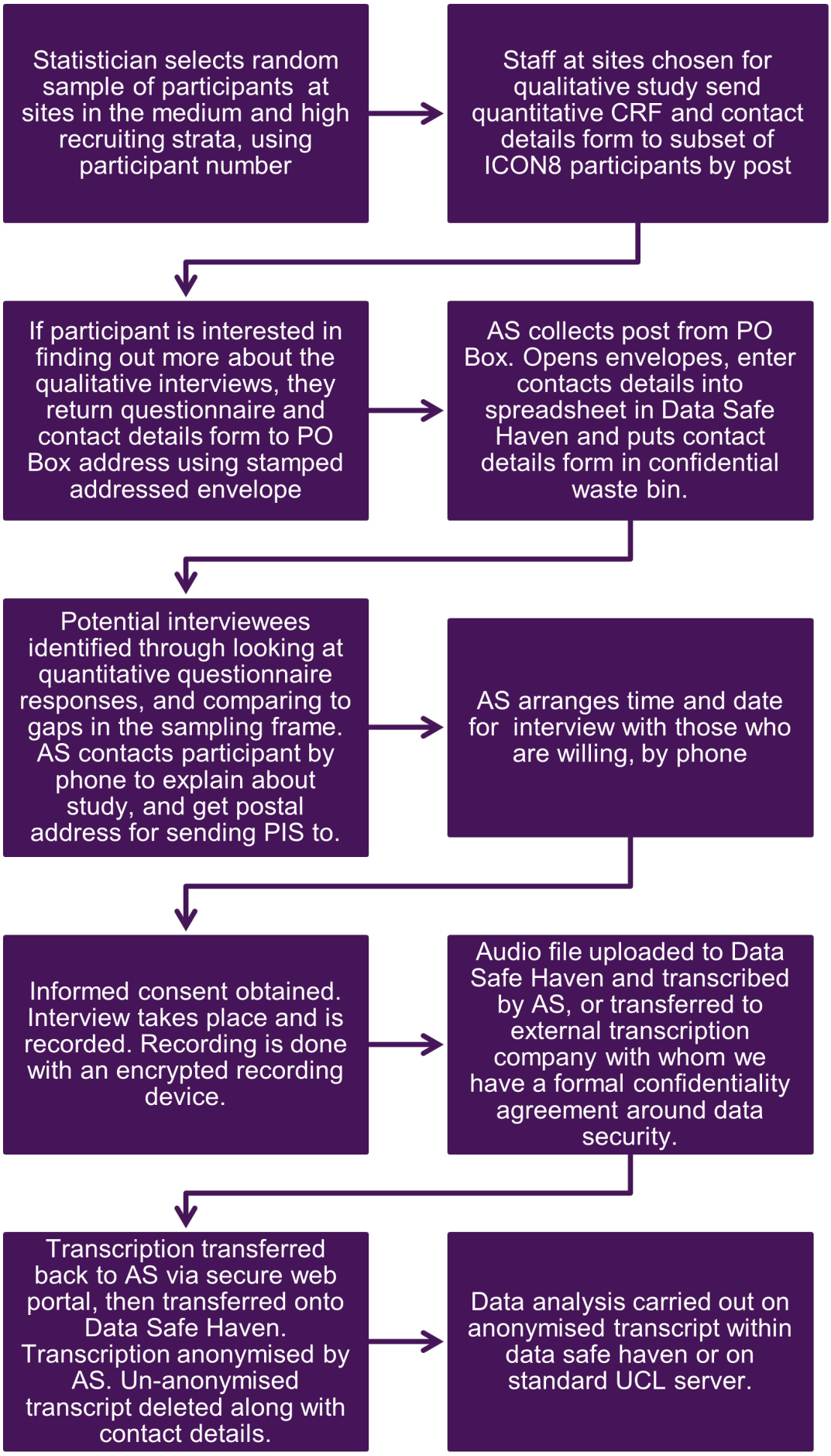
3.5 Data collection

3.5.1 Overview

As shown in Figure 3.1, data collection for the qualitative studies happened via semi-structured interviews and free-text questions on the quantitative patient and site staff questionnaires. Details about the data collection process for the questionnaires can be found in Section 2.10. Figure 3.2 gives an overview of the data collection process for patient data.

I carried out semi-structured interviews with participants either face-to-face, in the participant's own home or workplace (depending on whether the

Figure 3.2: Overview of the qualitative patient data collection process within Show RESPECT



interviewee was a patient or member of site staff), or by telephone. Interviews took place between April-September 2019.

3.5.2 Why chose interviews over focus group discussions?

The main source of qualitative data was semi-structured interviews with participants. I chose to use semi-structured interviews for data collection, as opposed to focus groups, for three reasons. The first reason relates to the nature of data I wanted to collect; I wanted to gather in-depth personal accounts of individuals' experiences of receiving or communicating trial results, and the factors that influence this, including personal context. This type of subject matter is well suited to exploration in a semi-structured interview, rather than focus group discussion, where the data is shaped by group interaction. It allowed me to explore individuals' experiences which were rare, for example I was able to explore the views of a patient who did not want to find out the results, and those of a patient who had wanted to find out the results but had not managed to. These perspectives might have been hard to explore within a focus group where most participants had very different experiences or views. The second reason for using individual interviews rather than group discussions was practical; my target participants were geographically dispersed over a wide area. Patient participants had ovarian cancer, and, for some, their health may have made travel to a group discussion impractical. Some patient participants had jobs or caring responsibilities that would have made scheduling a group discussion challenging. Site staff have clinical commitments, so finding a suitable time and date that would work for enough people would be very difficult. Using individual interviews allowed me to find times that were convenient for my participants. The third reason (for the patient participants) was the potentially sensitive nature of the topic. Ovarian cancer is a serious health condition. Recounting experiences around treatment, trial participation and receiving trial results may be upsetting for some patients. Individual interviews allowed me to respond to individual's emotional needs more easily than had I been facilitating a focus group discussion. For site staff, using individual interviews may help participants express opinions that they felt could go against the views of colleagues.

3.5.3 Collecting free-text responses alongside the quantitative data

Alongside the qualitative interviews, I collected some qualitative data from free-text questions on the questionnaires that were completed by patients and site staff. The free text questions were related to the more quantitative questions, allowing the participants to explain why they selected a certain box, or raise issues that may be important to them, but which were not adequately covered by the quantitative questions. The patient questionnaire can be found in

Annex 1, the Site staff CRFs can be found in Annex 2 and the CTU staff CRFs in Annex 3. While questionnaires are likely to collect lower quality data than other qualitative data collection approaches[101], I felt that it was appropriate to include free-text questions to allow respondents an opportunity to express their views beyond simply picking a categorical option. The qualitative data collected through the questionnaires allowed me to incorporate views from a larger number of participants in my qualitative studies than would be feasible through interviews alone, although the data collected through the questionnaires is necessarily less rich than that collected through interviews.

3.5.4 Consent

For the interviews, participants who agreed to be contacted about the qualitative study were sent the qualitative study participant information sheet and consent form. I answered any questions by telephone, and, if the patient or site staff member was willing to take part, a time, date and location for the interview was arranged. At the start of the interviews, I went through the information sheet with the patient or site staff member, answered any questions and made sure they understood what was involved. I then obtained informed consent from the participant, taking one signed copy of the consent form, and leaving the participant with a copy for their records. For interviews that took place remotely via telephone, I contacted the participant a week ahead of the interview by telephone to go through the information sheet and consent forms with the interviewee, and answer questions. The interviewee was then asked to post the signed consent form, to reach me prior to the interview commencing. At the start of the interview, I checked whether there are any further questions, and made sure the interviewee was still happy to take part in the interview.

Section 2.5.2 describes the consent process for the questionnaires.

3.5.5 Data collection instruments

The topic guides for the patient and site staff interviews can be found in Annex 4 and Annex 5, respectively. Interviews were conducted either in person, or over the telephone, and recorded on an encrypted recording device. Data were collected between December 2018 to September 2019 (pre-COVID-19).

3.5.5.1 Patient and public involvement to inform the patient topic guide

In order to inform the development of the interview topic guide for patient interviews, I held a PPI discussion group for women taking part in ovarian cancer trials. I asked them what factors were likely to influence how trial participants felt about how results are shared with them. Attendees highlighted various issues, listed below in the priority order they identified.

- Wording used
- Amount of information
- Relationship with who tells you the information
- How the overall results fit with your personal experience during the trial
- How simple/complex the information is (in relation to your own level of understanding)
- How the results were communicated (mode)
- Access to further support in dealing with the results
- Whether you feel like you've helped other people through your participation
- How well you are when you receive the communication
- Which group of the trial you were in
- Whether you feel your contribution was valued
- Your own stage in your treatment pathway (e.g. if you have just started treatment, or if you have nearly run out of options)
- If there is information about side effects that you personally experienced
- Timing of information
- Whether the communication is personal or generic

The topic guide was drafted to allow for these issues to be explored. Once the topic guide had been drafted, I talked through it by telephone with two ovarian cancer patients (separately) to get their views on whether it was clear, and whether any aspects were likely to be upsetting for participants, and how to minimise this risk. The topic guide was then further revised, and submitted to ethics.

3.5.5.2 Structure of the patient topic guide

The topic guide started with introductory information about the research and interview process, and seeking informed consent. It then explored participants' experiences of seeking and obtaining health information generally, followed by their experience of being part of the ICON8 trial. It then went on to explore their experience of finding out the ICON8 results (or not finding out, as appropriate). Patients were then asked about their understanding and interpretation or the ICON8 results (if they had received them). Patients were then asked to look at and give their views on the different Show RESPECT interventions. I then asked their views on sharing trial results with people who were not on the trial. Participants were then asked if they had any advice for researchers, or other things they would like to say about the topic. I finished the interview by thanking the participant, giving them a voucher as a thank you, asking if they had any questions, and offering them contact details for relevant local and national support groups.

3.5.5.3 Site staff topic guide

The topic guide started with introductory information about the research and interview process. It then went on to ask the site staff member about their role generally, and on the ICON8 trial and Show RESPECT studies specifically, along with information such as how many other trials they work on and in which disease areas. It then asked them about their own experiences of finding out the results of trials they have worked on, and previous experiences of sharing trial results with participants. I then asked them about their views about sharing results with trial participants in general, including whether they thought participants wanted to know, and concerns and perceived benefits of sharing results. We then went on to explore the practicalities of sharing the ICON8 results, before discussing any response they had received from ICON8 participants. I then asked for their views on the approaches used to share the ICON8 results, starting with the interventions their site had been randomised to, moving on to the other interventions in Show RESPECT. I then asked their views about future practice in this area, and any recommendations they would make for others. I finished the interview by thanking the participant and answering any questions they had.

3.5.5.4 Refining the topic guide

The topic guides were amended as interviews proceeded to follow-up on issues that emerged in early interviews, and to improve clarity[102]. The topic guide was also amended for interviews where the participant had not already learnt the results, taking out the questions about their experience of receiving the results. For participants who did not want to find out the results, the topic guide was abridged so they were not asked to look at any of the results summaries.

The quantitative questionnaires contained some free-text questions, giving participants the opportunity to say why they selected a particular quantitative response, and add further comments. The questionnaires for patients, site staff and CTU staff can be found in Annex 1, Annex 2 and Annex 3, respectively.

3.7 Data processing

3.7.1 Interview data

Interviews were transcribed using an ‘intelligent verbatim’ approach, whereby ‘filler’ words such as ‘um’ and ‘err’ were omitted, as this type of detail was not required for the analysis[103]. I transcribed the first two interviews, following which a professional transcription company transcribed the remaining interviews. Upon receipt of the transcriptions, I listened to the audio recording

while reading the transcript, to check for and correct inaccuracies. I replaced details that might potentially enable identification of the interviewee, such as names, details revealing the hospital or location, or other potential identifiers in the transcript with a generic description (such as "[hospital name]") to anonymise it.

Audio recordings from the interviews are stored on the UCL Data Safe Haven, along with transcripts prior to anonymisation. Anonymised transcripts for analysis are stored on UCL servers, and only members of the Show RESPECT team directly involved in this aspect of the study have access to it. The anonymised transcripts were then imported into Atlas.ti software as individual documents, labelled with key characteristics of the participant in terms of the factors in the sampling frame.

3.7.2 Questionnaire data

Section 2.10 describes the data entry process for entering questionnaire data (which includes the free text fields) onto the study database, and the quality assurance process that I used to check this was carried out accurately. Data were exported from the database in a format that could be imported into Stata version 16.1, which was used for the quantitative analysis. Free-text data, along with respondent characteristics, were exported from Stata as a csv file to be imported into Atlas.ti. Potential identifiers such as site, date of birth, or ICON8 patient ID were removed.

3.8 Ethical considerations

Section 2.13 describes the approvals obtained for the study.

There was a risk that participants in the qualitative study could find the interviews emotionally difficult. To mitigate this, I ensured that participants were fully informed about the topic of the interview as part of the informed consent procedure. I tried to be sensitive to the needs and emotions of the interviewee, reminding participants they could pause or end of the interview at any time, or skip any questions if they wish to do so. At the end of the interview I offered patients contact details for ovarian cancer helplines (Target Ovarian Cancer and Ovacome) and local support groups. The Participant Information Sheet explained that if I became concerned that the interviewee needed immediate support, I would refer them to their GP/site team/emergency mental health team, as appropriate.

3.9 Analysis

3.9.1 Coding and developing themes

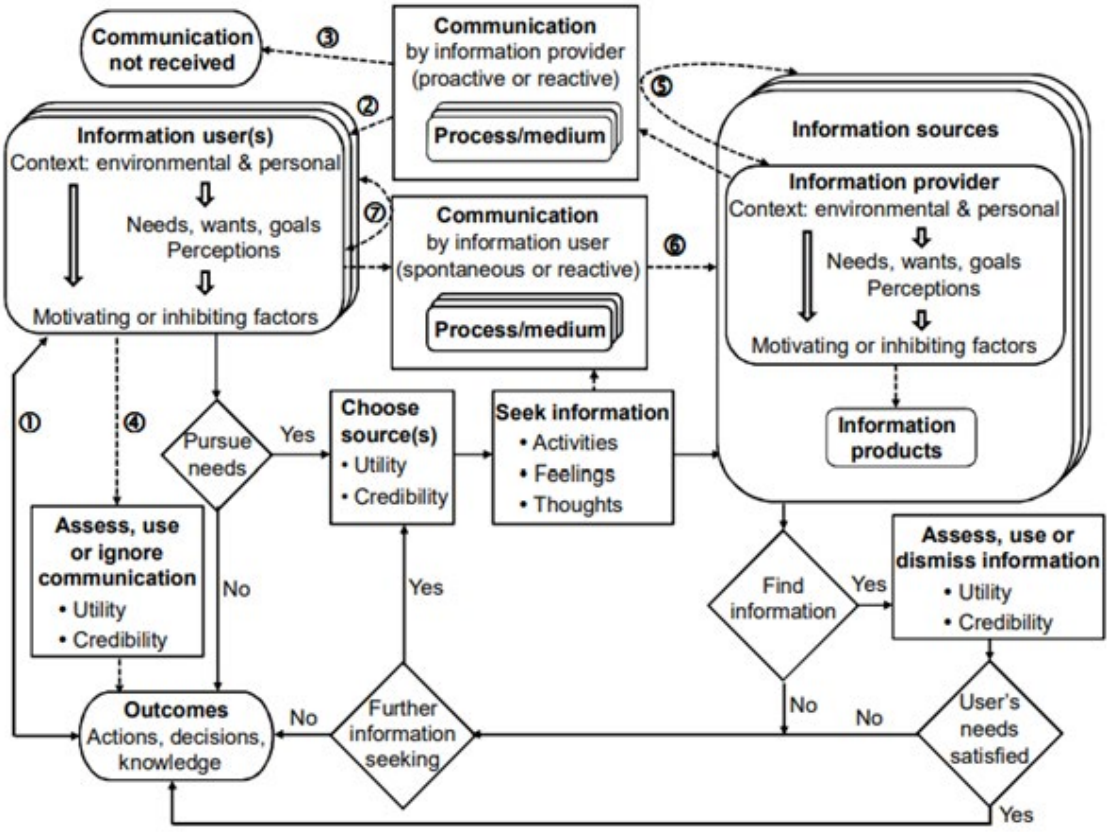
I used a reflexive thematic analysis approach to analyse the qualitative data [104]. Analysis started with the interview data. I read the transcript while listening to the audio recording of the interview. I then coded the transcript using a combination of inductive codes (generated from the data) and deductive codes (from a priori concepts in the topic guide and research questions), within the software Atlas.ti version 8.4. Quotations were given as many codes as were appropriate to cover the content of the quotation.

After nine interviews had been coded, with 569 detailed codes created, I printed off the list of codes and cut them up so each code was on a separate piece of paper. I then moved around the pieces of paper until the individual codes were grouped into initial themes, where each of the codes in the group related to a core concept. For example, all the codes that related to actions site staff took, or participants thought should be taken, to prepare patients to receive the results, were grouped into a theme called 'Preparing participants to receive results'. This included discussions at the informed consent stage, helping participants understand the potential outcomes of the trial, phoning participants to let them know the results were coming, and the role of the Patient Update Information Sheet in preparing patients. This process of grouping codes allowed me to identify that there were several duplicate codes, which covered the same concept but were named differently. I then grouped the codes in Atlas.ti, using the code name to indicate the theme as well as the code. I also merged duplicate codes (after checking that the data in both codes to be merged really did relate to the same concept). I then continued to code additional transcripts and the free-text data from the questionnaires.

My review of more than 50 potentially relevant theoretical frameworks, identified from the research communication and knowledge transfer literatures, alongside my initial coding of around half the transcripts, led me to decide to apply the Information Seeking and Communication Model (ISCM)[105, 106] (Figure 3.3) as a framework for high-level categorisation and conceptualisation of my data. The model covers the perspective of both the Information User (patients) and Information Provider (site staff), incorporating:

- the communication process,
- communication medium
- information product

Figure 3.3: The Information-Seeking and Communication Model[106]



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- the context in which the Information User and Information Provider are operating,
- what the Information User does to process that information,
- the outcomes receiving that information.

I mapped my initial themes and codes onto concepts from the Information Seeking and Communication Model, moving codes to different themes where they fitted better. Most of my codes fitted within the model, requiring only minor adaptation of the model, as discussed in Section 10.5.8. Annex 6 contains a table showing my themes and high-level codes, and the Information Seeking and Communication Model concepts they relate to.

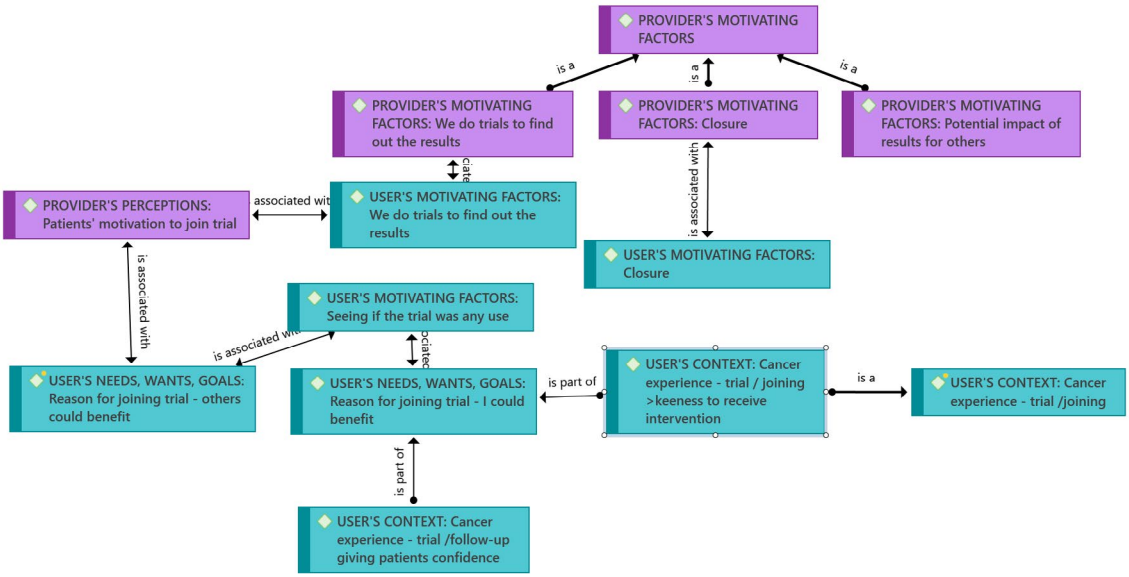
Once analysis of all the interview transcripts for a respondent type (patient or site staff) was completed, I imported free text responses from the questionnaires for that respondent type into the Atlas.ti project, and coded them using the same coding scheme as the interview data, with additional codes added where necessary.

As my analysis progressed, I refined my codes, themes and sub-themes. For example, having initially categorised data relating to the different

communication interventions in Show RESPECT in separate sub-themes for each intervention, I subsequently rearranged codes contained within these themes to become part of sub-themes that cut across the different interventions, within an overarching theme of 'Views on the Show RESPECT interventions.' The initial themes defined by each intervention were then scrapped, and codes relating to the information contained within the information products were moved to a separate theme focusing on the information being communicated.

Once coding was complete, I created network diagrams to explore linkages between codes within each candidate theme and sub-theme. I imported all the codes that may relate to a candidate theme or sub-theme into the diagram, moving them around to group closely related codes. I read and compared quotations linked to all the codes within the network to check for consistency of meaning for each code, and created links between related codes (such as one code being associated with another, being an example of something described by another, higher-level code, or being the opposite of or contradicting another code). Where a theme or sub-theme included data from both site staff and patients, I looked at the quotations by type of respondent, to see how their perspectives compared (in Figure 3.4, codes relating to data from site staff are coloured purple, and from patients coloured green). Figure 3.4 is one example of a network created at this stage of the analysis, showing codes relating to the theme of patients' motivation for joining the trial, and how this links to patients' desire to receive results. This example is chosen as it is one of the simpler networks I produced, making it easier to read within the confines of an A4 page. At this stage of the analysis I identified several codes that could be merged. I wrote analytical memos to describe the findings for each sub-theme,

Figure 3.4: Example of a network diagram created during the analysis process



and refined theme and sub-theme names based on these network diagrams and the content of the analytical memos. My results chapters discuss themes organised by the research question to which they relate.

My themes were shaped by my research questions, emergent concepts from my qualitative data, the Information Seeking and Communication Model, and also, for Chapter 5 and Chapter 6, by my quantitative data, because of my choice of triangulation approach (Section 3.2.5). Using a 'Following the thread' approach to triangulation meant that I interrogated my qualitative data to shed light on findings from the quantitative data, so the quantitative questions fed into how my qualitative data were analysed and written-up for Chapter 5 and Chapter 6.

Analysis of the patient data took place between May 2019 and May 2021.

3.9.2 Ensuring the credibility of my findings

As described in Section 3.2.5, I used methods triangulation, comparing data collected by qualitative and quantitative methods. I also employed source triangulation, comparing data from semi-structured interviews and free-text responses within the questionnaire. I collected data from patients and site staff, allowing me to triangulate the perspectives of these different stakeholders to provide a broader understanding of the topic than would be possible with just one type of respondent.

I did not employ member checking directly with the people who participated in Show RESPECT. However, I did hold a PPI discussion group with women who were participants in ovarian cancer trials, to share the emerging findings with them, get their feedback on the results and interpretation, and implications for future trials. I also held meetings with site staff to share the initial findings with them, and get their feedback on interpretation and the implications of these findings. I also discussed initial findings with the ICON8 trial team, who suggested further ideas to explore within the qualitative analysis.

3.10 Reflexivity/positionality

I am a highly educated, white woman in my late thirties, with a decade of experience at communicating the results of clinical trials. I think that being the same gender as most of my interviewees helped with putting interviewees at their ease, especially as many of the patient interviews were conducted in their homes – this might have been difficult had I been male.

I have a public health background, but no clinical training. I do not have personal experience of ovarian cancer, but have a friend who has ovarian cancer and has taken part in several trials. I have been a trial participant (for

a less serious condition), and have also taken part in several observational studies, and have experience of receiving the results of those studies in different ways.

I am an introvert, which I think helped with the interviewing, as I was comfortable leaving silences while participants thought, rather than jumping in with the next question straight away. This quite often led to interviewees giving additional insights on a question, which might have been lost had I asked the next question without a pause. This was harder to do in the telephone interviews, when there was no body language to read.

I designed the Show RESPECT study because, based on my experience of talking to trial participants, I believed that most trial participants want to be offered the results of trials they had taken part in, and that this does not happen well enough in many trials. Prior to conducting the interviews and analysis, I expected that the printed summaries would be the intervention that was preferred by trial participants. This was based in part on my knowledge of the literature in this area, and also because it is accessible to all and not dependent on computer literacy and access to the internet. I thought the opt-out approach was also likely to mean more patients who wanted to know the results actually finding them out. I also expected the enhanced webpage to be superior to the basic webpage in terms of the primary outcome of Show RESPECT, and preferred by patients. I knew from the monitoring data we collected as Show RESPECT progressed that there had been very few people visiting the link to sign up to the email list. I tried not to let my presuppositions influence my interviewing, by asking open questions, and, in analysis, by checking for data that went against my assumptions.

My views on the interventions shifted somewhat during the process of data collection. By the end of data collection, I still expected the printed summary to improve satisfaction, particularly given the importance of keeping records of their treatment that many participants demonstrated. However, my expectations around the outcomes of the enhanced webpage lessened, as through the interviews it became clear that while patients liked the idea of many of the 'enhanced' features (FAQ section, video, links to further information and support), this was more because they thought it might benefit others, rather than themselves.

I was the Chief Investigator of the Show RESPECT study, and also designed the interventions that were being tested. When preparing for the interviews, I was concerned that this would lead to interviewees being unwilling to say negative things about the interventions or process used within Show RESPECT. I was also concerned that patients would be unwilling to recount

negative experiences about ICON8 if they thought I was connected to their research nurse or trial doctor. When introducing myself and my role to patient interviewees, I explained that I was a researcher from UCL. I explicitly said that I was not part of their hospital's team. I did not reveal that I had been involved in developing the Show RESPECT communication materials, and they did not seem to assume that I had. I think this approach was successful at encouraging patients to be open with me about their views on the interventions. This was helped by showing them several different interventions within the interview. This gave them an opportunity to compare the different interventions, and say what they preferred about one over another, providing a non-confrontational way for them to reveal what they disliked about any particular intervention.

The site staff I interviewed were aware of my role within the Show RESPECT study, as they had taken part in Site Initiation training that I had led, and had also received emails from me in my role as study Chief Investigator. This may have made it harder for them to criticise the interventions tested. I think allowing them to compare the interventions tested within Show RESPECT, and talk about their previous experience from other trials, helped give them opportunities to express concerns and reservations about the approaches used in Show RESPECT. They were also able to talk about what they thought patients might think, rather than what they thought, which may have made it easier to criticise the interventions without worrying about causing offense.

I carried out the interviews before the statistical analysis was carried out, but I had seen the quantitative data as it came in, so I was aware of some of the issues that emerged from the free-text questionnaire responses. I did not know which intervention was associated with highest satisfaction. However, qualitative analysis was carried out both before and after the quantitative results were known.

4. Show RESPECT Interventions

4.1 Overview of scope of this chapter

This chapter describes the communication interventions that were tested in Show RESPECT, including the process of selecting the interventions, their development, and the process of delivering the interventions within Show RESPECT.

4.2 Selecting the interventions

In Show RESPECT I wanted to test interventions that would be feasible for trials without access to extensive communications expertise at the CTU level to implement. For the results to be of relevance to other trials, the interventions also needed to be ones that sites working within the NHS could deliver to participants. These two principles guided the selection of approaches for testing within Show RESPECT.

As described in Section 1.6, my initial review of the literature revealed that a number of approaches to sharing results had been used in other settings, including:

- Written summaries or letters sent by post[13-15, 19, 20, 37, 42, 43, 45-47]
- Individual telephone calls[13, 44, 46]
- Teleconferences[44]
- Group meetings between patients and local trial staff[40, 43, 45]

Individual or group telephone calls or meetings have potential advantages in terms of allowing participants to ask questions, however the resources required for these approaches may be prohibitive. Individual telephone calls or meetings with clinicians were likely to be infeasible for sites for most MRCCTU trials, which often have many hundreds or even thousands of participants. Previous experience has shown us that participant meetings are resource intensive, often reach relatively few participants and are impractical for large trials with many sites.

Electronic means of communication, such as websites, email, online forums or social media offer a number of potential advantages, such as:

- potentially straightforward to implement
- low-cost
- reduce burden on sites
- enable participants to opt-in
- offer opportunities to share information in a number of ways, including text, images, audio and video

Online methods are likely to be increasingly used to share trial results with participants, however there is currently little evidence on how acceptable or effective they are. There have been few studies reported so far investigating the use of these methods for sharing results with participants[42, 43, 45, 48]. Some pharmaceutical companies have recently developed online portals for participants to access trial results[33]. The EU are also developing a portal that trialists will be required to post a lay summary of their results to, as part of the new EU Clinical Trial regulation[58].

There are concerns around the accessibility of online communication methods for some patient populations. The UK government's Digital Divide research shows that, in 2018, around 10% of the adult UK population were "internet non-users", meaning people who never use the internet, or who have not used it in the last three months. People over the age of 65 were more likely to be internet non-users[107]. This may make online methods less appropriate for trials with a high proportion of participants aged 65 or older.

4.2.1 Patient and public involvement to inform intervention choices

During a PPI focus group I co-organised with Cancer Research UK, I asked participants (split into two groups) to sort the different approaches to sharing results with participants into categories of 'preferred', 'acceptable' or 'unacceptable'. Where members of the group held different opinions, this was recorded. Both groups identified some kind of written summary as one of the preferred approaches – in group 1 all chose emailed written summaries, and in group 2, printed summaries posted to participants and written summaries on a website were selected as preferred approaches. Group 2 noted that printed summaries may be more inclusive, particularly for people who do not have access to the internet/email. Group 1 also identified a couple of interactive approaches as preferred, including a meeting with other trial participants where a doctor presents the results, and teleconferences that participants can dial into anonymously. However, it was felt that in some circumstances people may prefer a 1:1 meeting or teleconference rather than a face-to-face group meeting.

There were concerns with the individual interactive methods of communication (calls from research nurses or face to face meetings with clinicians) regarding feasibility. This led to several participants saying these methods were unacceptable. Another concern with individual calls from nurses was fear of having to wait around for a phone call, rather than having a set time to dial into a teleconference. Another spoke of the frustration experienced when a phone call with results was promised but never happened.

There was a general consensus that a combination of methods should be used, perhaps using a staged approach where they can read the results at home first, before engaging with the more interactive approaches such as meetings or teleconferences. One participant commented that a film or teleconference or webinar would be brilliant after they had heard the initial results.

I then carried out a PPI survey of 76 patients to find out which modes of communication were most of interest as a way of sharing results with trial participants. Survey respondents were asked to rank the following approaches according to how they thought people taking part in a clinical trial would prefer to be told the results:

- A printed summary of the results, posted when the main results are published (most preferred or second most preferred by 52% of respondents)
- Two printed summaries sent by post: one with early results and one with more detail, when that is available (most preferred or second most preferred by 50% of respondents)
- Having the option to sign up to an email list, which will be used to send summaries of the results and links to further information (most preferred or second most preferred by 46% of respondents)
- Having a link to a webpage with a summary of results plus links to additional information such as patient support groups (most preferred or second most preferred by 38% of respondents)
- A private online forum where results will be posted, and participants can ask questions and discuss the results (most preferred or second most preferred by 13% of respondents)
- Being invited to a teleconference where researchers will explain the results, and people are able to ask questions (most preferred or second most preferred by 9% of respondents)

Additional ways of sharing results suggested by respondents included noticeboards at hospitals/GP surgeries, one-to-one by a research nurse or consultant, discussion group or meeting, and text messages with links to a webpage.

The results of the survey encouraged us to drop the web forum, as it was unpopular with most respondents, and likely to be resource intensive to set-up. We continued to consider the teleconference as an option, given the patient population for the ICON8 trial was older women, and giving an option that did not rely on reading skills or computer literacy might be valuable for this population.

Once the host trial for Show RESPECT had been determined, I ran a PPI discussion group for women taking part in ovarian cancer trials. One of the aims of this discussion group was to gather more specific guidance from our target patient population to inform our intervention choices. At that point in the trial development process, we were considering four interventions: printed summary sent by post, email list, webpage and teleconference. Attendees were generally positive about the interventions, except for the teleconference, which was not popular. It was felt that teleconferences would be particularly difficult for any patients who were undergoing second-line chemotherapy. Based on feedback from this group, and the PPI survey, we decided to drop this intervention.

The result of this patient and public involvement was the following interventions were chosen to test within Show RESPECT:

- An 'enhanced' webpage featuring a short video of a clinician summarising the results; diagrams; links to further information and support; and a section on Frequently Asked Questions, enabling participants to send in questions to be answered on the webpage
- An opt-out Posted Printed Summary of the results
- An email list to receive a summary of the results by email, along with answers to questions sent in by participants

4.3 Selecting the 'control'

We decided that the control for Show RESPECT needed to be some kind of results summary, rather than no summary at all, as we felt that it would be unethical to randomise some patients to not receive the results. We know from the literature that around nine in ten trial participants want to be informed of trial results, and that it is supported in guidance around the ethical conduct of trials (see Section 1.3). We therefore decided that all patients should be offered at least a webpage containing a plain language summary of the results. This summary used the structure of plain language summaries mandated in the European Clinical Trials Directive[58]. This is an appropriate control, as, once this aspect of the Directive is in force, this will be a way that all participants in clinical trials carried out in the EU will, in theory, be able to access the results. However, this basic results summary structure does not take advantage of some of the features that communicating via the internet allows. The structure is also not specifically aimed at trial participants, so misses pieces of information that may be important to them.

4.4 Development of the interventions

The structure of the three interventions (Enhanced Webpage, Printed Summary and Email), was based on an adapted version of the template in the MRCT Return of Aggregate Results guidance[32]. The adaptations I made were based on experience from previous trials, where PPI input had shown that other information not covered in the MRCT template was of interest to participants. Table 4.1 compares the structure of the different interventions and that of the MRCT Return of Aggregate Results template version 2.0. Text was drafted for the interventions applying principles of writing in plain language.

Once I had drafted the text for the interventions, it was reviewed for accuracy and comprehensibility by:

- a member of staff from the Target Ovarian Cancer information service
- a patient representative on the Show RESPECT steering group
- the ICON8 trial management team

I then got feedback on the revised, formatted printed summary from the ovarian cancer discussion group. Their feedback included discussion of how progression free survival was explained – the draft they saw used a plain language definition used by Cancer Research UK. The original wording (borrowed from the Cancer Research UK trials database) was “improve how long women with ovarian cancer lived, and delay the disease getting worse”. The discussion group felt that this made it seem that it was inevitable that the disease was going to get worse, so for the version that was used in Show RESPECT we changed this to “delay (or prevent) the cancer coming back or getting worse and improve how long women with ovarian cancer lived”. Another change they suggested was making the thank you at the end of summary more prominent by giving it a heading. The summary text was revised again in the light of these comments, and went to the ICON8 team for final approval before being submitted for ethics approval.

4.5 Description of the interventions

Table 4.2 provides a comparison of the two Show RESPECT webpages using the TIDIER framework[108]. Links to the basic webpage and enhanced webpage are contained in the table. Table 4.3 provides a description of the printed summary using the TIDIER framework, and Table 4.4 describes the Email list intervention. The Printed Summary is appended in Annex 7, and the email in Annex 8 of this thesis.

Table 4.1: Comparison of the structures of the Basic Webpage, Enhanced Webpage, Printed Summary, Email and MRCT Return of Aggregate Results template

Basic webpage	**Enhanced webpage**	**Printed summary**	**Email**	**MRCT Return of Aggregate Results template v2.0**
Study Name	Thank you	Thank you	Thank you	Thank you for participating in this study
	Quick links to information on this page		What's in this email?	
Who Sponsored this study?	What was the ICON8 trial about?			Why the study was done
General information about the study	Why was the ICON8 trial needed?			Study information
What patients were included in this study?	Who took part in the ICON8 trial?			How the study worked
Which medicines were studied?	How was the ICON8 trial carried out?			
What were the side effects?	What did the ICON8 trial find?			Side effects
What were the overall results of the study?				Summary of results
How has this study helped patients and researchers?	How sure can we be about these results?			Final comments
Are there plans for further studies	What do these results mean • For you? • For other people?			
Where can I find further information about this study?	What difference will these results make?			
	Thank you			
	Further information			
	Support		Any questions?	
	Frequently asked questions		Support	
	Tell us what you think about this webpage		Tell us what you think about this email	

Table 4.2: Comparison of the webpages tested in Show RESPECT

	Basic webpage	Enhanced webpage
Why	European Parliament Regulation (EU) No 536/2014 Article 37 (4) requires sponsors to provide summary results of clinical trials in a format understandable to laypersons. These summaries will be made available in a new EU database[58]. The regulation specifies 10 items that should be included in the summary. The 'friendly' version of these items has been used to structure the basic webpage content, as this is the format in which lay summaries will be available for EU trials once the database is launched, and is therefore the minimum that will be available to participants.	The enhanced webpage was designed to take advantage of some of the opportunities afforded by webpages to include different sorts of content in addition to static text. It was also written specifically for participants, rather than lay audiences in general, using a structure adapted from the MRCT guidance document v2.0[32]. It was hypothesised that adding these additional elements, and restructuring the results summaries specifically for participants, would increase participant satisfaction with how the results were communicated.
Materials	Participants received a printed update information sheet thanking them for taking part in the trial, telling them that the results were available, and how to access them (including a link to the webpage). Table 4.1 contains a description of the structure of the webpages.	
	The web page was be laid out with clear headings. The body text was Arial 12pts, black against a white background. Section 10 of the webpage contained a link to the entry on the clinical trial register. Text was written using the principles of Plain English. https://www.mrcctu.ucl.ac.uk/studies/all-studies/i/icon8/results-of-the-icon8-trial-1/	In addition to written content, the enhanced webpage contained a short video of a trial clinician explaining the results. The enhanced webpage also contained two diagrams. The frequently asked questions section contained a link to an online form where participants could post anonymous questions about the results, to be answered in that section of the webpage. The web page was be laid out with clear headings. The body text was Arial 14pxs, black against a white background. Text was written using the principles of Plain English. Section 11 contained links to the Cancer Research UK's page about ICON8, the clinical trial register entry for ICON8, information about ovarian cancer from ovarian cancer charities https://www.mrcctu.ucl.ac.uk/studies/all-studies/i/icon8/results-of-the-icon8-trial/

	Basic webpage	Enhanced webpage
Procedures	The Patient Update Information Sheet was sent to all participants at sites randomised to the printed summary, giving them the link to the webpage.	
		Questions about the results could be submitted anonymously via an online form using the Opinio survey system. When questions were received, answers were drafted and posted onto the webpage within three weeks.
Who provided	The Patient Update Information Sheets were provided by staff at the participant's trial site. This was usually a research nurse or trial administrator. The webpages were hosted on the MRC Clinical Trials Unit at UCL's website.	
Modes of delivery	For most participants the Patient Update Information Sheet was delivered by post to the participants' home address. For a few, where clinic visits coincided with when the documents were due to be sent, they were given in person. The webpage was then available on the internet.	
Where the intervention took place	At participants' homes.	
When and how much	One Patient Update Information Sheet (2 pages) was sent. Participants could then access the webpage as often as they liked, for as long as they liked.	
Tailoring	Some sites sent a personalised cover letter or compliments slip with the Patient Update Information Sheet, giving their contact details for if patients had any questions about the results. Some sites phoned patients to tell them they would be sending the Patient Update Information Sheet. Some sites did no tailoring.	
Modifications	Sites were not able to modify the Patient Update Information Sheet or webpage.	
	The content of the webpage remained unchanged.	The webpage was updated with answers to questions received via the online form.
How well	All eligible patients (with one exception) were sent the Patient Update Information Sheet which contained the link to the webpage.	
	The link to the basic webpage for two sites was broken for a week in February 2019 (affecting up to 4 patients).	The link to the enhanced webpage for two sites was broken for 10 days in February 2019 (affecting up to 5 patients).

Table 4.3: Description of the Printed Summary

Why	As the population of women taking part in ICON8 had an average age of >60, it was thought that lack of computer literacy might act as a barrier to some patients accessing the results via webpage or email. A Printed Summary might avoid these challenges. Previous studies have seen low uptake of results when participants have to opt-in to receive them[46], so it was decided to make the Printed Summaries opt-out. The text was also written specifically for participants, rather than lay audiences in general, using a structure adapted from the MRCT guidance document[32]. It was hypothesised that providing the results in printed format to all participants who did not opt out would improve satisfaction compared to not offering a printed summary.
Materials	Participants received a Patient Update Information Sheet thanking them for taking part in the trial, telling them that the results were available, and how to access them. This included a link to whichever webpage they had been randomised to. They were also told that they would be sent a Printed Summary of the results in three weeks time, unless they let their study team know that they did not wish to receive this. The structure of the printed summary is shown in Table 4.1 The content of the printed summary was written following the principles of Plain English. The text of sections 2-10 was identical to that of the enhanced webpage. It contained information on relevant patient helplines, and the link to the trial registry entry. The Printed Summary was laid out with clear, colour headings, plenty of white space, and the body text was Arial 12pts, black against a white background. It used graphics to illustrate key points. It was four A4 pages long. It was professionally printed on 150gsm paper.
Procedures	The Patient Update Information Sheet was sent to all ICON8 participants at sites randomised to the Printed Summary, telling them they would be sent the Printed Summary in three weeks unless they opted out. The Printed Summary was then sent to participants who had not opted out.
Who provided?	The Patient Update Information Sheets and Printed Summaries were provided by staff at the patient's trial site. This was usually a research nurse or trial administrator.
Modes of delivery	For most participants the Patient Update Information Sheet and Printed Summary were delivered by post to the participants' home address. For a few, where clinic visits coincided with when the documents were due to be sent, they were given in person.

Where the intervention took place	At participants' homes.
When and how much	One Patient Update Information Sheet (2 pages) was sent. For patients who did not opt out, a four-page Printed Summary was sent three weeks later.
Tailoring	Some sites sent a personalised cover letter or compliments slip with the Patient Update Information Sheet and Printed Summary, giving their contact details for if patients had any questions about the results. Some sites phoned patients to tell them they would be sending the Patient Update Information Sheet and Printed Summary. Some sites did no tailoring.
Modifications	Sites were not able to modify the Patient Update Information Sheet or Printed Summary. The content of the Printed Summary remained the same throughout the course of the study.
How well	All eligible patients at sites randomised to the Printed Summary were sent the Patient Update Information Sheet, which informed them they would be sent the Printed Summary in three weeks time unless they opted out. Three patients opted out of receiving the Printed Summary. All other eligible patients were sent the Printed Summary.

Table 4.4: Description of the Email List intervention

Why	The email list was designed to offer participants the opportunity to receive content similar to the enhanced webpage directly to their inbox. This was particularly relevant for responses to any frequently asked questions, to save participants having to regularly check the webpage for updates. The content of the results email was the same as the enhanced webpage, minus the video. The content of subsequent emails was the same as the frequently asked question updates of the enhanced webpage.
Materials	Participants received a Patient Update Information Sheet thanking them for taking part in the trial, telling them that the results were available, and how to access them. This included a URL to a form where participants could enter their email address onto a secure MailMan database, which was not linked to their trial data. The email updates were designed using a MailChimp template that works well in different email platforms, including mobile phones. The structure of the first email is described in Table 4.1 Subsequent emails included answers to questions sent in by participants, and links to previous emails. The content of the emails was written following the principles of Plain English. The emails were be laid out with clear headings, plenty of white space, and the body text was Arial 12pts, black against a white background.
Procedures	The Patient Update Information Sheet was sent to all participants at sites randomised to the printed summary, giving them the link to sign up to the email list. When participants signed up to the email list, they were sent an email, confirming their subscription and telling them how they can unsubscribe at any time. The first email with a summary of results (using the same written content as the enhanced webpage,) was sent 1 month after the first sites randomised had received the Patient Update Information Sheets, to allow them time to distribute them to participants, and for participants to sign up. Questions about the results could be submitted anonymously via an online form using the Opinio survey system. Update emails were sent out with answers to any frequently asked questions that have been received since the previous email, and any updates. Participants who signed up to the email list after the first email had been sent were sent a welcome email with a link to online copies of any email(s) that have previously been sent.

Who provided?	The Patient Update Information Sheets were provided by staff at the patient's trial site. This was usually a research nurse or trial administrator.
Modes of delivery	For most participants the Patient Update Information Sheet was delivered by post to the participants' home address. For a few, where clinic visits coincided with when the documents were due to be sent, they were given in person. Sign-up to the email list was via a webpage. Emails were then sent to email addresses.
Where the intervention took place	At participants' homes.
When and how much	One Patient Update Information Sheet (2 pages) was sent. Patients who signed up for the email list were then sent a confirmation email. The first email with a summary of results (using the same written content as the enhanced webpage,) was sent 1 month after the first sites randomised had received the Patient Update Information Sheets, to allow them time to distribute them to participants, and for participants to sign up. Update emails were sent out with answers to any frequently asked questions that had been received since the previous email, and any updates. Only one email update was sent, with answers to 5 questions sent in by one participant. Participants who signed up to the email list after the first email had been sent were sent a welcome email with a link to online copies of any email(s) that have previously been sent.
Tailoring	Some sites sent a personalised cover letter or compliments slip with the Patient Update Information Sheet, giving their contact details for if patients had any questions about the results. Some sites phoned patients to tell them they would be sending the Patient Update Information Sheet. Some sites did no tailoring.
Modifications	Sites were not able to modify the Patient Update Information Sheet or email. Additional emails were sent based on questions received from participants.
How well	All eligible patients at sites randomised to the email list were sent the Patient Update Information Sheet which contained the link to sign up to the email list.

4.6 Process of delivering the interventions

I developed a 2-page Patient Update Information Sheet (see Annex 9) to provide patients with information on how to access the webpage they had been randomised to, or, if applicable, sign up to the email list, or opt out of receiving the Printed Summary. This was based on the HRA End of Study Information Sheet template[109]. It contained the following information:

- Study title
- Introduction

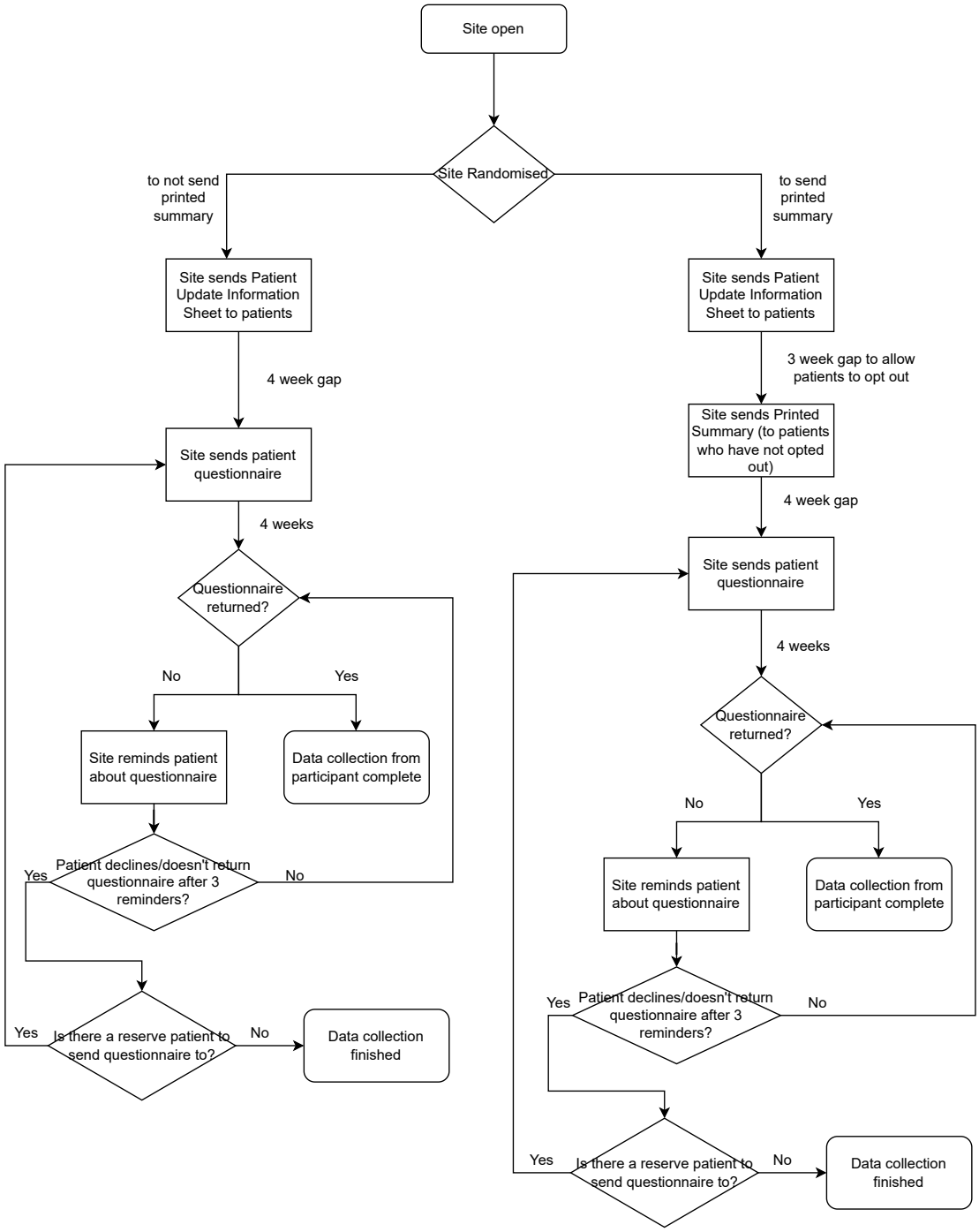
- Thank you
- What is happening now in the ICON8 study?
- How can I report side-effects?
- What results will be available and when?
- How can I find out the results of the research?
- Will I be given any results about me as an individual?
- Which group of the study was I in?
- If I have any questions, whom should I contact?
- Further information

Sites were asked to send all ICON8 participants a site-specific Patient Update Information Sheet containing information on how to access the results specific to that site's randomisation. Sites that were randomised to the Printed Summary then waited for three weeks, to give participants the chance to opt out of receiving the Printed Summary, before sending the Printed Summary by post to all eligible participants who had not opted out. Figure 4.1 gives an overview of the intervention and data collection process for sites. Sites completed logs at each stage of this process, so we could keep track of whether the interventions were being delivered as planned to eligible participants.

As part of the site set-up process, site staff involved in Show RESPECT received training which covered:

- The rationale for the study
- The study design
- The outcomes the study was assessing
- Study procedures, including logs, randomisation and the process outlined in Figure 4.1
- Data collection and site questionnaires
- Timelines
- Site payment
- Adverse events
- The qualitative component of the study

Figure 4.1: Intervention and data collection process



5. Patients' perspectives on the effectiveness of the Show RESPECT interventions

5.1 Overview of the scope of this chapter

This chapter reports patient data from Show RESPECT, including both quantitative and qualitative data. It starts by summarising the number of sites and patients that took part in Show RESPECT. It then describes delivery of the interventions within Show REPECT and the baseline characteristics of patient participants. Results relating to the primary outcome of the study, participant satisfaction with how the results were shared, are explored, together with qualitative data on the reasons for satisfaction or dissatisfaction. I then explore uptake of the Show RESPECT interventions, following by whether the information told participants everything they wanted to know; whether it was understandable; whether it was easy to find; and patients' attitudes to trial participation. Quantitative and qualitative findings relating to the same issues are alongside each other using a 'following the thread' triangulation approach (see Section 3.2.5). Quotes from patients are shown in indented, blue italic text. This chapter concludes with a short discussion of these results, including key findings, strengths and limitations. These results were published in *PLoS Medicine* in October 2021[110]. I led the analysis and writing of that paper.

Results relating to the information contained within the summaries and the information products used to convey the results are discussed in Chapter 8. Participants' reaction to the results are discussed in Chapter 7. Other factors that influence satisfaction with how the results are shared are discussed in Chapter 9.

5.2 Results

5.2.1 Participation in Show RESPECT

The 83 ICON8 sites in the UK were assessed for eligibility. Forty sites were excluded for reasons including lack of ICON8 participants eligible for Show RESPECT (5), lack of capacity (6), declining to take part (4), failing to obtain site approvals in time (12) or non-response to the invitation (13). 43 (52%) ICON8 UK sites took part in Show RESPECT. Figure 5.1 shows the CONSORT diagram for the study. Table 5.1 shows the number of sites randomised to the interventions by site size strata, the number of eligible patients who were offered the interventions, sent the questionnaire, and returned the questionnaire. Data collection took place between December 2018 and

Chapter 5 Summary Box

Why was this study done?

- Previous research has shown that most people who take part in clinical trials want to be told the results of those trials, but many participants never get to find them out.
- There is little evidence to guide researchers on how best to share results with the people taking part in their trials.

What did I do?

- I collected and analysed quantitative and qualitative data from patients participating in ICON8, covering their views and experiences on how the ICON8 trial results were shared with them

What did I find out?

- **Nine in ten women wanted to be told the results** of the trial they had taken part in
- **Women at hospitals which were randomised to the posted printed summary (in addition to a webpage) were more likely to be satisfied** with how the results were shared and were **more likely to find out the results** than those at hospitals not randomised to the posted printed summary
- Women who received the results said that **the information was easy to understand and find**, and **told them everything they wanted to know**
- Participants said they were **likely to take part in future research and recommend it to others**

What do these findings mean?

- These findings suggest that trials with similar participants to our ovarian cancer trial (mainly women aged fifty or older), where webpages are used to share results with people taking part, should also share results through opt-out mailed printed summaries
- This will enable more people who want to know the results to find them out, and improve satisfaction

September 2019. In total, 384 ICON8 participants were offered the Show RESPECT interventions; 275 were sent the questionnaire of which 180 returned the questionnaire (65%).

Figure 5.1 CONSORT diagram for Show RESPECT patient participants

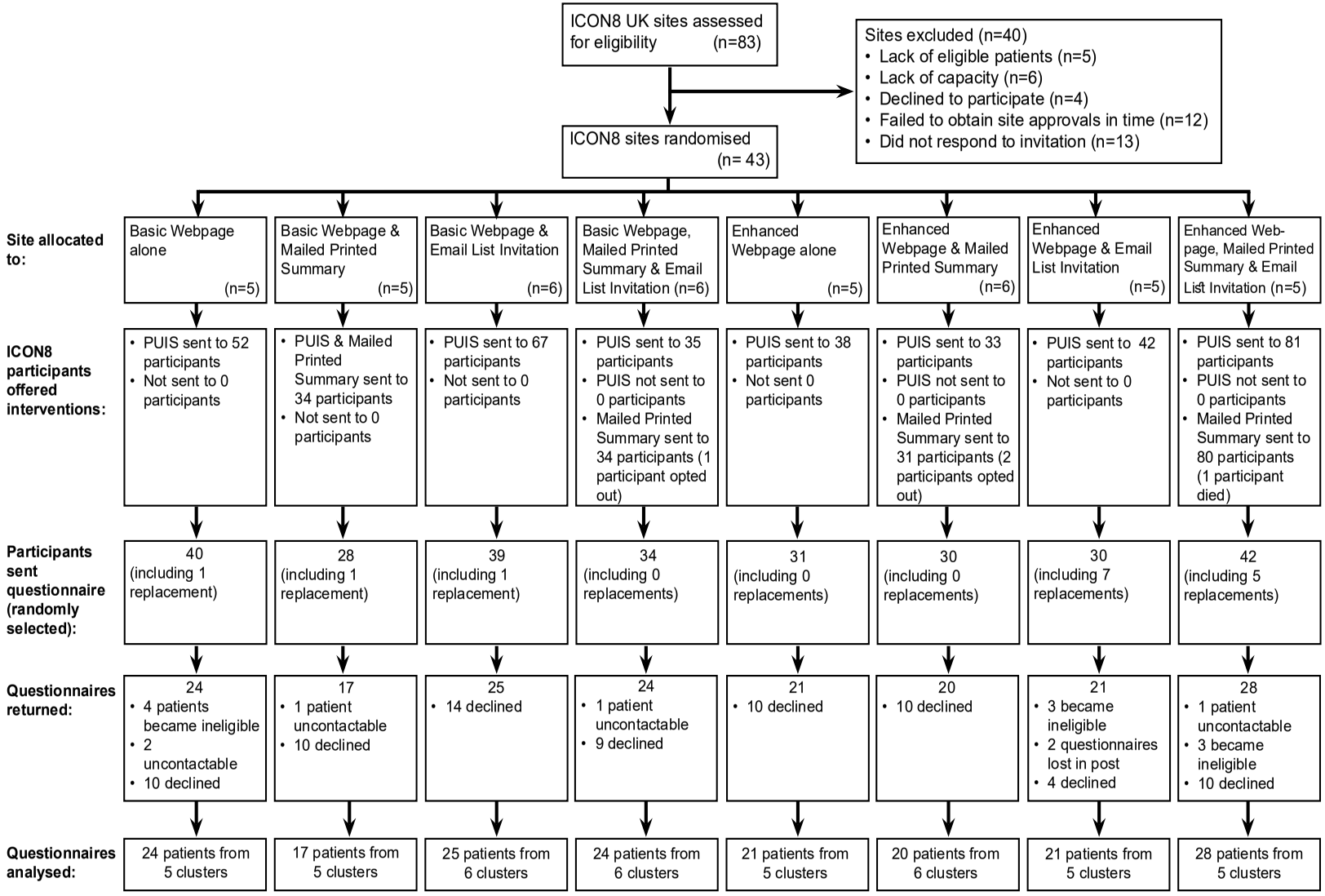


Table 5.1: Recruitment of sites and participants to Show RESPECT, by site size[1]

	Overall	Webpage		Posted Printed Summary		Email List Invitation	
		Basic webpage	Enhanced webpage	No Posted Printed Summary	Posted Printed Summary	No Invitation	Invitation
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of sites							
TOTAL	43	22	21	21	22	21	22
Small sites	17 (40)	8 (36)	9 (43)	8 (38)	9 (41)	9 (43)	8 (36)
Medium sites	13 (30)	7 (32)	6 (29)	6 (29)	7 (32)	6 (29)	7 (32)
Large sites	13 (30)	7 (32)	6 (29)	7 (33)	6 (27)	6 (29)	7 (32)
Number of eligible participants (offered interventions)							
TOTAL	384	190	194	201	183	157	227
Small sites	54 (14)	24 (13)	30 (15)	27 (13)	27 (15)	32 (20)	22 (10)
Medium sites	76 (20)	45 (24)	31 (16)	37 (18)	39 (21)	35 (22)	41 (18)
Large sites	254 (66)	121 (64)	133 (69)	137 (68)	117 (64)	90 (57)	164 (72)
Number of participants sent the questionnaire							
TOTAL	275	142	133	141	134	129	146
Small sites	53 (19)	24 (17)	29 (22)	26 (18)	27 (20)	31 (24)	22 (15)
Medium sites	67 (24)	40 (28)	27 (20)	30 (21)	37 (28)	33 (26)	34 (23)
Large sites	155 (56)	78 (55)	77 (58)	85 (60)	70 (52)	65 (50)	90 (62)
Number of participants who returned the questionnaire (number analysed)							
TOTAL	180	90	90	91	89	82	98
Small sites	40 (22)	15 (17)	25 (28)	21 (23)	19 (21)	21 (26)	19 (19)
Medium sites	49 (27)	30 (33)	19 (21)	23 (25)	26 (29)	26 (32)	23 (23)
Large sites	91 (51)	45 (50)	46 (51)	47 (52)	44 (49)	35 (43)	56 (57)

[1] Small sites had 5 or fewer ICON8 patients, Medium sites 6-12 ICON8 patients, and large sites 13 or more ICON8 patients alive at the time of the site agreeing to be part of Show RESPECT.

	Overall	Webpage		Posted Printed Summary		Email List Invitation	
		Basic webpage	Enhanced webpage	No Posted Printed Summary	Posted Printed Summary	No Invitation	Invitation
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Response rate (percent of questionnaires sent that were returned)							
TOTAL	65%	63%	68%	65%	66%	64%	67%
Small sites	75%	63%	86%	81%	70%	68%	86%
Medium sites	73%	75%	70%	77%	70%	79%	68%
Large sites	59%	58%	60%	55%	63%	54%	62%

5.2.2 Delivery of the interventions

Logs kept by sites showed that Patient Update Information Sheets went to 100% of eligible ICON8 participants at participating sites. Three ICON8 participants opted out of receiving the Posted Printed Summary, and one ICON8 participant died after the Patient Update Information Sheet was sent and before the Posted Printed Summary was sent. According to site logs, all other eligible ICON8 participants at sites randomised to Printed Summaries were sent the Posted Printed Summary.

5.2.3 Characteristics of participants

The mean age of patients who returned the questionnaire was 67, with approximately one third from each of the three ICON8 arms. There was a wide range of reported highest level of educational qualification, with 38 (21%) reporting no qualifications, and 41 (23%) holding a degree or higher qualification. Nearly all participants who returned the questionnaire reported English being their first language. 61 (40%) respondents reported using the internet or email less frequently than every day, with 26 (15%) never using internet or email. The baseline characteristics of those who returned the questionnaire can be seen in Table 5.2, and Table 5.3 shows the baseline characteristics of all eligible ICON8 participants at Show RESPECT sites.

94 participants were invited to take part in the qualitative study, of whom 13 (14%) were interviewed. Table 5.4 shows the characteristics of the interviewed participants. Only 3/185 participants randomised to the Posted Printed Summary opted out of receiving it, none of whom were at sites taking part in the qualitative study. No participants signed up to the Email List. Only 5 respondents to the quantitative questionnaire were aged 50 or younger, of whom only one was at a site taking part in the qualitative study. This meant I was unable to recruit participants for these parts of the sampling frame: 'opted out of Posted Printed Summary', 'had used the Email List' and 'aged 50 or younger'.

5.2.4 Did the interventions improve satisfaction with how the results were shared?

5.2.4.1 Quantitative findings on satisfaction with how results were shared

Table 5.5 shows the patient-reported outcomes relating to the experience of receiving the results, by intervention (Webpage, Printed Summary, Email). The Posted Printed Summary led to a large difference in satisfaction with how results were communicated (adjusted ordinal OR 3.15, 95% CI 1.66 to 5.98, $p<0.001$). There was no evidence of differences in satisfaction for

Table 5.2: Baseline characteristics of participants who returned the questionnaire

	Overall	Webpage		Posted Printed Summary		Email List Invitation	
	n (%)	Basic webpage n (%)	Enhanced webpage n (%)	No Posted Printed Summary n (%)	Posted Printed Summary n (%)	No Invitation n (%)	Invitation n (%)
Age							
Mean (IQR)	67 (62-74)	68 (62-74)	67 (61-74)	68 (62-74)	68 (63-75)	67 (61-73)	67 (62-74)
≤70 years	103 (57)	51 (57)	52 (57)	51 (57)	43 (52)	60 (61)	103 (57)
>70 years	77 (43)	39 (43)	39 (43)	38 (43)	39 (48)	38 (39)	77 (43)
ICON8 arm							
Standard treatment	57 (32)	26 (29)	31 (34)	29 (32)	28 (31)	25 (30)	32 (33)
Dose fractionated paclitaxel	61 (34)	33 (37)	28 (31)	32 (35)	29 (33)	28 (34)	33 (34)
Dose fractionated carboplatin & paclitaxel	62 (34)	31 (34)	31 (34)	30 (33)	32 (36)	29 (35)	33 (34)
Highest level of educational attainment							
No qualifications	38 (21)	14 (16)	24 (27)	25 (27)	13 (15)	19 (23)	19 (20)
GCSE or equivalent	57 (32)	28 (31)	29 (33)	26 (29)	31 (36)	32 (40)	25 (26)
A-level or equivalent	42 (24)	25 (28)	17 (19)	18 (20)	24 (28)	17 (21)	25 (26)
Undergraduate degree	24 (13)	11 (12)	13 (15)	11 (12)	13 (15)	8 (10)	16 (16)
Postgraduate degree	17 (10)	11 (12)	6 (7)	11 (12)	6 (7)	5 (6)	12 (12)

	Overall	Webpage		Posted Printed Summary		Email List Invitation	
	n (%)	Basic webpage n (%)	Enhanced webpage n (%)	No Posted Printed Summary n (%)	Posted Printed Summary n (%)	No Invitation n (%)	Invitation n (%)
English as first language							
Yes	172 (97)	82 (93)	90 (100)	85 (96)	87 (98)	78 (98)	94 (96)
No	6 (3)	6 (7)	0 (0)	4 (4)	2 (2)	2 (3)	4 (4)
Use of internet or email							
Never	26 (15)	17 (19)	9 (10)	13 (14)	13 (15)	11 (13)	15 (15)
Once per month at most	7 (4)	3 (3)	4 (4)	4 (4)	3 (3)	6 (7)	1 (1)
More than once per month, but not as often as every week	11 (6)	1 (1)	10 (11)	6 (7)	5 (6)	0 (0)	11 (11)
Once per week or more, but not as often as every day	27 (15)	10 (11)	17 (19)	15 (17)	12 (13)	16 (20)	11 (11)
Every day	108 (60)	58 (65)	50 (56)	52 (58)	56 (63)	49 (60)	59 (61)

Table 5.3: Baseline characteristics of all eligible participants at trial sites

	Webpage		Posted printed summary		Email list	
	Basic webpage n (%)	**Enhanced webpage n (%)**	**No printed summary n (%)**	**Printed summary n (%)**	**No invitation n (%)**	**Invitation n (%)**
Age						
Mean (IQR)	67 (61-74)	66 (58-73)	66 (59-73)	67 (60-74)	67 (61-74)	66 (59-73)
≤70 years	115 (58%)	121 (63%)	125 (62%)	111 (60%)	90 (57%)	146 (63%)
> 70 years	82 (42%)	71 (37%)	78 (38%)	75 (40%)	68 (43%)	85 (37%)
ICON8 arm						
Standard treatment	58 (29%)	67 (35%)	63 (31%)	62 (33%)	50 (32%)	75 (32%)
Dose fractionated paclitaxel	73 (37%)	62 (32%)	72 (35%)	63 (34%)	53 (34%)	82 (35%)
Dose fractionated carboplatin & paclitaxel	66 (34%)	63 (33%)	68 (33%)	61 (33%)	55 (35%)	74 (32%)

(NB. Not all of these participants were sent the questionnaire – see Section 2.10 for more details).

Table 5.4: Characteristics of qualitative interviewees

Characteristics	No. of interviewees
Total number of interviewees	13
Interventions offered[1]	
Basic Webpage	8
Enhanced Webpage	5
Posted Printed Summary	6
No Posted Printed Summary	7
Email List	9
No Email List	4
Interventions used[2]	
Basic Webpage	5
Enhanced Webpage	2
Posted Printed Summary	6
Opted out of Posted Printed Summary	0
Email List	0
Had not found out the results prior to interview	2
Reported satisfaction with how the results were shared (from quantitative questionnaire)[3]	
Very unsatisfied, quite unsatisfied or neither satisfied nor unsatisfied	5
Quite satisfied or very satisfied	5
Reported highest level of education[4]	
A levels or lower	6
Degree or higher	6
Reported frequency of internet/email use	
Less than once a week	2
More than once a week	11
ICON8 randomised allocation	
Three-weekly chemotherapy (control arm)	3
Weekly chemotherapy (intervention arms)	10
Age group	
≤50	0
51-60	2
61-70	6
≥71	5

1 Adds up to >13 as some participants were offered more than one intervention

2 Adds up to >13 as some participants used more than one intervention

3 Data missing from 3 participants' questionnaires

4 Data missing from 1 participant's questionnaire

Table 5.5: Reported outcomes relating to experience of receiving the results by randomised intervention

	Webpage			Posted Printed Summary (PPS)			Email List			
	Basic n (%)	**Enhanced** n (%)	**Unadjusted OR (uOR)[1] (95% CI) p-value Adjusted OR (aOR)[2] (95% CI) p-value**	**No PPS** n (%)	**PPS** n (%)	**Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value**	**No Invitation** n (%)	**Invitation** n (%)	**Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value**	**Overall n (%)**
Reported satisfaction with how the results were communicated										
Very unsatisfied	6 (9)	6 (8)	uOR:1.39 (0.75 to 2.59) p=0.295 aOR: 1.47 (0.78 to 2.76) p=0.235	6 (9)	6 (7)	uOR: 3.27 (1.74 to 6.16) p<0.001 aOR: 3.15 (1.66 to 5.98) p<0.001	8 (12)	4 (5)	uOR: 1.33 (0.71 to 2.47) p=0.373 aOR: 1.38 (0.72 to 2.63) p=0.327	12 (8)
Quite unsatisfied	8 (12)	4 (5)		7 (11)	5 (6)		8 (12)	4 (5)		12 (8)
Neither	11 (16)	6 (8)		12 (19)	5 (6)		8 (12)	9 (11)		17 (12)
Quite satisfied	16 (23)	24 (32)		23 (36)	17 (21)		13 (20)	27 (34)		40 (28)
Very satisfied	28 (41)	36 (47)		16 (25)	48 (59)		29 (44)	35 (44)		64 (44)
The information told me everything I wanted to know[3]										
Strongly disagree	0 (0)	3 (4)	uOR: 2.13 (1.13 to 4.00) p=0.019 aOR: 2.15 (1.13 to 4.07) p=0.019	0 (0)	3 (4)	uOR: 1.32 (0.70 to 2.46) p=0.391 aOR: 1.32 (0.70 to 2.48) p=0.394	1 (1)	2 (3)	uOR: 1.12 (0.60 to 2.10) p=0.728 aOR: 1.11 (0.58 to 2.12) p=0.759	3 (2)
Slightly disagree	5 (7)	2 (3)		1 (2)	6 (7)		3 (4)	4 (5)		7 (5)
Neither	16 (23)	10 (13)		15 (23)	11 (14)		13 (19)	13 (16)		26 (18)
Slightly agree	21 (30)	13 (17)		20 (31)	14 (17)		16 (24)	18 (23)		34 (23)
Strongly agree	28 (40)	48 (63)		29 (45)	47 (58)		34 (51)	42 (53)		76 (52)
The information was easy to understand[3]										
Strongly disagree	2 (3)	4 (5)	uOR: 0.92 (0.47 to 1.81) p=0.817 aOR: 1.05 (0.53 to 2.08) p=0.895	1 (2)	5 (6)	uOR: 1.60 (0.82 to 3.11) p=0.167 aOR: 1.66 (0.84 to 3.27) p=0.144	2 (3)	4 (5)	uOR: 0.85 (0.43 to 1.66) p=0.627 aOR: 0.79 (0.39 to 1.59) p=0.500	6 (4)
Slightly disagree	4 (6)	1 (1)		2 (3)	3 (4)		3 (4)	2 (3)		5 (3)
Neither	10 (14)	8 (11)		12 (18)	6 (7)		8 (12)	10 (13)		18 (12)
Slightly agree	10 (14)	16 (21)		14 (22)	12 (15)		10 (15)	16 (20)		26 (18)
Strongly agree	44 (63)	47 (62)		36 (55)	55 (68)		44 (66)	47 (59)		91 (62)

	Webpage			Posted Printed Summary (PPS)			Email List			
	Basic n (%)	**Enhanced** n (%)	**Unadjusted OR (uOR)[1] (95% CI) p-value Adjusted OR (aOR)[2] (95% CI) p-value**	**No PPS** n (%)	**PPS** n (%)	**Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value**	**No Invitation** n (%)	**Invitation** n (%)	**Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value**	**Overall n (%)**
It was easy to find the trial results										
Strongly disagree	5 (7)	3 (4)	uOR: 1.34 (0.71 to 2.53) p=0.373 aOR: 1.75 (0.90 to 3.42) p=0.100	3 (5)	5 (6)	uOR: 1.15 (0.61 to 2.18) p=0.662 aOR: 1.37 (0.71 to 2.66) p=0.345	5 (8)	3 (4)	uOR: 0.81 (0.42 to 1.54) p=0.511 aOR: 0.70 (0.36 to 1.38) p=0.306	8 (6)
Slightly disagree	5 (7)	4 (5)		7 (11)	2 (3)		4 (6)	5 (6)		9 (6)
Neither	14 (21)	7 (9)		6 (9)	15 (19)		6 (9)	15 (19)		21 (15)
Slightly agree	8 (12)	19 (25)		14 (22)	13 (16)		11 (17)	16 (20)		27 (19)
Strongly agree	36 (53)	43 (57)		34 (53)	45 (56)		39 (60)	40 (51)		79 (55)

[1] Adjusted for strata, randomisation phase (early vs late) and clustering

[2] Adjusted for age, education level and internet use as well as strata, randomisation phase (early vs late) and clustering

[3] For producing the odds ratios for this variable, the strongly and slightly disagree categories were merged.

the Enhanced vs Basic Webpages (adjusted OR 1.47, 95% CI 0.78 to 2.76, p=0.235) and Email List vs No Email List (adjusted OR 1.38, 95% CI 0.72 to 2.63, p=0.327). There was no evidence of interaction between any pair of interventions.

When the seven possible combinations of interventions were looked at individually, compared to the control of basic webpage alone, the only combinations for which there was evidence of improved satisfaction were the ones that included the Posted Printed Summary Table 5.6).

5.2.4.2 Patients' views on the reasons for satisfaction with how results were shared

Participants valued the information contained in the results summaries being clear and understandable (see Section 5.2.7.2 for more information on understandability of the information), and the results being interesting (see Section 7.6.4 for more information on participants' emotional response to the results). Some participants (all from sites allocated to the printed summary) said they were satisfied with how the results were shared because they had received information in their preferred way, with having a physical document making it easier to access, read and keep the information (see Sections 5.2.8 and 8.2.1 for further discussion of this). Other participants said their satisfaction was because of the thoughts and feelings the results provoked, including reassurance, putting their own experiences in context, and knowing that they had not been forgotten about. Participants also wrote about the impact they thought the trial would have for future patients as a reason for their satisfaction with receiving the results. The process of informing participants that the results were available (through the Patient Update Information Sheet), before the results were shared was appreciated by some patients.

> *"I found the whole experience very professional and reassuring." ELQ04: Patient, large site randomised to Enhanced Webpage only*
>
> *"Easy to understand and work out where I personally fitted into the results" DMQ07: Patient, medium site randomised to Basic Webpage, Printed Summary & Email List Invitation*
>
> *"Good to know that the trial could help experts decide how to move forward with treatment for the future" DMQ02: Patient, medium site randomised to Basic Webpage, Printed Summary & Email List Invitation*
>
> *"It was helpful being informed the results were on the way so I was prepared and looked out for them" DMQ09: Patient, medium site randomised to Basic Webpage, Printed Summary & Email List Invitation*

Table 5.6: Effect of combinations of interventions on satisfaction with how the results were shared

	Very unsatisfied	Quite unsatisfied	Neither satisfied nor unsatisfied	Quite satisfied	Very satisfied	Unadjusted OR[1] (vs basic webpage alone) (95% CI) p-value	Adjusted OR[2] (vs basic webpage alone) (95% CI) p-value
Basic webpage alone	2 (13)	4 (25)	5 (31)	2 (13)	3 (19)	-	-
Basic webpage & printed summary	2 (13)	1 (7)	0 (0)	4 (27)	8 (53)	**5.66 (1.47 to 21.81) p=0.012**	**5.34 (1.38 to 20.63) p=0.015**
Basic webpage & email list	1 (6)	1 (6)	4 (25)	7 (44)	3 (19)	1.77 (0.53 to 5.91) p=0.352	1.65 (0.46 to 5.90) p=0.439
Basic webpage & printed summary & email list	1 (5)	2 (9)	2 (9)	3 (14)	14 (64)	**7.71 (2.21 to 26.89) p=0.001**	**7.91 (2.22 to 28.20) p=0.001**
Enhanced webpage alone	2 (13)	1 (6)	2 (13)	4 (25)	7 (44)	2.94 (0.81 to 10.62) p=0.101	2.85 (0.78 to 10.37) p=0.112
Enhanced webpage & printed summary	2 (11)	2 (11)	1 (5)	3 (16)	11 (58)	**5.12 (1.39 to 8.93) p=0.014**	**5.05 (1.36 to 18.75) p=0.016**
Enhanced webpage & email list	1 (6)	1 (6)	1 (6)	10 (63)	3 (19)	2.67 (0.80 to 8.93) p=0.111	3.10 (0.90 to 10.66) p=0.072
Enhanced webpage & printed summary & email list	1 (4)	0 (0)	2 (8)	7 (28)	15 (60)	**7.21 (2.20 to 23.69) p=0.001**	**7.09 (2.16 to 23.27) p=0.001**

[1] Adjusted for strata, randomisation phase (early vs late) and clustering

[2] Adjusted for age, education level and internet use as well as strata, randomisation phase (early vs late) and clustering

5.2.4.3 What caused some participants to be unsatisfied with how the results were shared?

Reasons for dissatisfaction with how the results were shared, included: not knowing how to find out the results; problems accessing the webpage (Section 5.2.8); finding the results difficult to understand (Section 5.2.7); perceived lack of timeliness in receiving the results; and the information not giving enough detail (Section 5.2.6).

Some participants said they would have preferred to have found out the results in a different way. For example, some who had not been randomised to the Posted Printed Summary said they would have preferred to receive the results by post, rather than having to go online. On the other hand, some who were randomised to the Posted Printed Summary would have preferred to receive results via a webpage or email (all participants had the option of receiving results via one of the webpages, but not all seem to have realised this). The perceived advantages to these electronic forms of communication were the ability to share with others, and saving NHS resources.

> *"The ways in which the results were sent through was overwhelming. Prefer to read webpage but don't know how to access it." BLQ03: Patient, large site randomised to Basic Webpage and Printed Summary*

> *"Would have preferred to get e-mail with results in rather than going on a webpage because people don't always remember to go to webpages" CLQ12: Patient, large site randomised to Basic Webpage and Email List Invitation*

5.2.5 Uptake of the Show RESPECT interventions

Nearly all patients (164/177 (93%)) reported wanting to know the ICON8 results, and 145 (88%) of these 164 reported finding out the results. None of the 13 patients who said they did not want to know the results reported having found them out. These 13 patients were spread across the Show RESPECT interventions. Section 7.4 explores the views of participants and site staff around patients' desire to know trial results.

The Posted Printed Summary significantly increased the odds of finding out the results among those patients who wanted to know, compared to No Posted Printed Summary. In the Posted Printed Summary arm 78/83 (94%) reported finding out the results, compared to 67/81 (83%) of those in the no Posted Printed Summary arms. This had an odds ratio (OR) of 3.57 (95% Confidence Interval (CI) 1.18 to 10.77, p=0.024), adjusted for age, education level, internet use, strata, randomisation phase and clustering (Table 5.7). There was no evidence of a difference in the proportion of those who wanted to receive the

Table 5.7: Proportion of patients who wanted to know the results reporting finding them out, by randomisation

	Webpage		Posted printed summary		Email list		Overall
	Basic webpage	Enhanced webpage	No printed summary	Printed summary	No invitation	Invitation	
	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Overall	71/80 (89)	74/84 (88)	67/81 (83)	78/83 (94)	65/74 (88)	80/90 (89)	145/164 (88)
Site size[1]							
Small	13/14 (93)	21/24 (88)	16/20 (80)	18/18 (100)	19/21 (90)	15/17 (88)	34/38 (89)
Medium	22/26 (85)	15/17 (88)	15/20 (75)	22/23 (96)	18/22 (82)	19/21 (90)	37/43 (86)
Large	36/40 (90)	38/43 (88)	36/41 (88)	38/42 (90)	28/31 (90)	46/52 (88)	74/83 (89)
Age							
≤70 years	42/45 (93)	43/48 (90)	41/48 (85)	44/45 (98)	33/38 (87)	52/55 (95)	85/93 (91)
>70 years	29/35 (83)	31/36 (86)	26/33 (79%)	34/38 (89)	32/36 (89)	28/35 (80)	60/71 (85)
ICON8 arm							
Standard treatment	16/20 (80)	21/75 (75)	16/24 (67)	21/24 (88)	17/20 (85)	20/28 (71)	37/48 (77)
Dose fractionated paclitaxel	29/31 (94)	24/26 (92)	28/30 (93)	25/27 (93)	24/27 (89)	29/30 (97)	53/57 (93)
Dose fractionated carboplatin & paclitaxel	26/29 (90)	29/30 (97)	23/27 (85)	32/32 (100)	24/27 (89)	31/32 (97)	55/59 (93)
Education level							
Up to A level	52/59 (88)	56/66 (85)	48/60 (80)	60/65 (92)	53/62 (85)	55/63 (87)	108/125 (86)
Degree or above	19/21 (90)	18/18 (100)	19/21 (90)	18/18 (100)	12/12 (100)	25/27 (93)	37/39 (95)
Use of internet/email							
Less than daily	24/28 (86)	32/37 (86)	27/32 (84)	29/33 (88)	24/29 (83)	32/36 (89)	56/65 (86)
Daily	46/51 (90)	42/47 (89)	39/48 (81)	49/50 (98)	41/45 (91)	47/53 (89)	88/98 (90)

[1] Small sites had ≤5 ICON8 patients, Medium sites 6-12 ICON8 patients, & large sites ≥13 ICON8 patients alive when the site agreed to be part of Show RESPECT.

results who actually found them out in the other randomisations (Enhanced vs Basic Webpage, or Email List Invitation vs No Email List Invitation).

Reported use of the Posted Printed Summaries was greater than that of the other interventions. Posted Printed Summaries were sent to 89 questionnaire respondents, 62 (70%) of whom reported using them, 10 (11%) reported not using them, and data were missing for the remaining 17 (19%). 23/90 (26%) participants randomised to the Basic Webpage and 28/90 (31%) randomised to the Enhanced Webpage reported using the webpage. 29/90 patients randomised to the Basic Webpage and 28/90 (31%) randomised to the Enhanced Webpage reported not using the webpage. However, data were missing on this question from 38/90 (42%) randomised to the Basic Webpage and 34/90 (38%) randomised to the Enhanced, making these results hard to interpret. No patients signed up to the email list.

5.2.6 Did the information tell patients everything they wanted to know?

Most patients agreed that the information told them everything they wanted to know (Table 5.5). Patients at sites randomised to the Enhanced Webpage were more likely to agree that the information told them everything they wanted to know (adjusted OR 2.15, 95% CI 1.13 to 4.07, p=0.019) than those allocated to the Basic Webpage. There was no evidence of differences in the proportion saying the information told them everything they wanted to know between the Posted Printed Summary versus No Posted Printed Summary (adjusted OR 1.32, 95% CI 0.70 to 2.48, p=0.394), or Email List versus No Email List (adjusted OR 1.11, 95% CI 0.58 to 2.12, p=0.759). Section 8.3 presents qualitative findings around the contents of the results summaries from both participants and site staff.

5.2.7 Was the information understandable?

5.2.7.1 Quantitative results on whether the information was understandable

80% of patients reported that they found the results easy to understand. There was no evidence of a difference in any of the randomised comparisons for this outcome (Table 5.5). The adjusted odds ratio for Enhanced vs Basic Webpage was 1.05 (95% CI: 0.53 to 2.08, p=0.895), Posted Printed Summary vs no Posted Printed Summary was 1.66 (95% CI: 0.84 to 3.27, p=0.144) and Email List Invitation vs no Email List Invitation was 0.79 (95% CI: 0.39 to 1.59, p=0.500). As an additional analysis which was not specified in the analysis plan, I looked at the proportion of participants who reported the results were easy to understand, by highest level of education. These results are shown in Table 5.8. There was no evidence of a difference in the proportion of people reporting the results were easy to understand by education level, with

most participants slightly or strongly agreeing that the results were easy to understand, regardless of their level of education. This was the case across all the interventions tested. Similarly, no evidence of differences were seen in reported understanding of the results by age group.

Table 5.8: Reported ease of understanding of the results by education level

	The trial results were easy to understand					
Highest level of education	Strongly disagree n (%)	Slightly disagree n (%)	Neither agree nor disagree n (%)	Slightly agree n (%)	Strongly agree n (%)	Total
No qualifications	2 (7)	0 (0)	6 (21)	6 (21)	14 (50)	28
GCSE / O-level / NVQ level 1	1 (2)	4 (8)	5 (10)	9 (18)	30 (61)	49
A-level / CSE / NVQ level 2	2 (7)	1 (3)	4 (13)	2 (7)	21 (70)	30
Degree	0 (0)	0 (0)	0 (0)	5 (25)	15 (75)	20
Postgraduate degree	1 (6)	0 (0)	3 (18)	2 (12)	11 (65)	17
Total	**6**	**5**	**18**	**24**	**91**	**144**

5.2.7.2 Patients' views on the understandability of the information

Patients generally described the information as "clear", "easy to understand" and not too "technical". However, some women did struggle to understand the results. For some, this difficulty in understanding the results lead them to be unsatisfied with how the results were communicated.

Nearly all the women I interviewed seemed to understand the results, and the summaries they gave of what the results showed, and their implications, were generally accurate reflections of the trial findings. However, for some patients, it had taken them a while to reach that understanding, with their understanding changing over time.

> *"Initially, when I first read it I was thinking I'm really glad I had the every three weeks because I thought the outcome would be better. But actually, when we looked at it again… And I haven't spoken to them since then because I'm not due to go back to see them again until next year. But having looked at it again, I can see basically, it didn't seem to make much difference whichever way the treatment was administered. It's just the different side effects from different dosages." DMI01: Patient, medium site randomised to Basic Webpage, Printed Summary and Email List Invitation*

Some women struggled with the amount of information given. Others struggled to understand that a trial might not produce a clear 'winner', so their understanding of what the results showed was accurate, but they were confused about the implications of that.

> *"I got a bit confused to be quite honest, because I didn't fully understand it. I came to the conclusion that the three different methods of*

administering the chemo didn't produce a winner, if you like. I got a bit lost after that as to where you went from there, because to me there hadn't been any great find; any big development." GMI01: Patient, medium site randomised to Enhanced Webpage and Email List Invitation

5.2.8 Was the information easy to find?

5.2.8.1 Quantitative results on how easy it was to find the information

Almost three quarters of patients reported easily finding the results, with no evidence of differences between any of the Show RESPECT interventions for this outcome (Table 5.5). The adjusted odds ratio for Enhanced vs Basic Webpage was 1.75 (95% CI: 0.90 to 3.42, p=0.100), for Posted Printed Summary vs no Posted Printed Summary was 1.37 (95% CI: 0.71 to 2.66, p=0.345) and Email List Invitation vs no Email List Invitation was 0.70 (95% CI: 0.36 to 1.38, p=0.306).

As an additional analysis which was not specified in the analysis plan, I looked at the proportion of participants who reported the results were easy to find, by reported frequency of internet/email use, age and education level. These results are shown in Table 5.9. People who used the internet daily were more likely to report that the results were easy to find. However, there was no evidence that those who used the internet less than daily found it easier to access results if they were randomised to the Posted Printed Summary. There was a suggestion that women over 70 years old were more likely to report that it was easy to find the results if they were randomised to the printed summary (72% agree/strongly agree in the Posted Printed Summary group vs 52%

Table 5.9: Reported ease of finding out the results, by subgroup

Highest level of education	The trial results were easy to find					Total
	Strongly disagree n (%)	Slightly disagree n (%)	Neither agree nor disagree n (%)	Slightly agree n (%)	Strongly agree n (%)	
Reported frequency of internet/email use						
Less than daily	6 (10)	5 (8)	17 (28)	12 (20)	20 (33)	60
Daily	6 (6)	6 (6)	11 (11)	16 (16)	59 (60)	98
Age group						
Up to 70 years old	5 (5)	5 (5)	16 (17)	13 (14)	53 (58)	92
More than 70 years old	7 (10)	6 (9)	12 (18)	15 (22)	27 (40)	67
Highest level of education						
No qualifications	3 (9)	2 (6)	6 (19)	7 (22)	14 (44)	32
GCSE / O-level / NVQ level 1	5 (9)	5 (9)	11 (21)	9 (17)	23 (43)	53
A-level / CSE / NVQ level 2	3 (9)	2 (6)	7 (21)	4 (12)	18 (53)	34
Degree	0 (0)	0 (0)	2 (10)	3 (14)	16 (76)	21
Postgraduate degree	1 (6)	2 (12)	2 (12)	3 (18)	9 (53)	17

agree/strongly agree in the No Posted Printed Summary group). There was no significant difference in reported ease of finding out the results by education level.

5.2.8.2 Patients' views on whether the information was easy to find

5.2.8.2.1 Accessibility of Posted Printed Summaries

The Posted Printed Summaries were seen as accessible to everyone, as they were not reliant on people's computer literacy or access to the internet. When asked whether there were other ways in which they would have liked to have received the results, 22/91 (24%) patients from hospitals not randomised to the Posted Printed Summary said they would have liked to receive the results by post, with post being seen as convenient and easier to access.

> *"Like my mum, for instance, in her 80s, she wouldn't have access to this [webpage], so she would only want… She would only be able to have posted results, really." GMI02: Patient, medium site randomised to Enhanced Webpage and Email List Invitation*

5.2.8.2.2 Not knowing how to access the results

Rarely, questionnaire respondents reported not having been told how to access the results. It is unclear whether or not they received the Patient Update Information Sheet (which site logs record as having been sent). Others (from sites not randomised to the Posted Printed Summary) reported receiving the Patient Update Information Sheet, but missed the information on how to obtain the results that the sheet contained.

> *"Apart from receiving the 'Patient Update' dated 11/5/2018 I have not been told anything else." CLQ02: Patient, large site randomised to Basic Webpage and Email List Invitation*

5.2.8.2.3 Accessibility of computer-based approaches to sharing results

In Show RESPECT, four out of every 10 patients reported using internet or email less than daily, and 15% reported never using internet or email. 11/180 questionnaire respondents reported difficulties accessing the webpage, either not having access to computers, or finding it hard to get onto the webpage, with some participants eventually gaining access, alone or with the help of family members, and others not succeeding. Having to go online to access results put some patients off from finding them out. Other patients, who had been able to access the results themselves, were concerned that sharing results via webpages/email alone would be inaccessible to other participants, either because of lack of computer literacy or lack of access to the internet.

> *"My daughter looked at the results on the webpage for me. I felt overwhelmed by the thought of using the website myself" AMQ07: Patient, medium site randomised to Basic Webpage only*

"I do understand why it's computer, because most people have computers nowadays. We have one, but I'm always sort of frightened, a bit frightened of them because I don't know what I'm doing, and I'll be looking at it and thinking, what do you do here? Which do you press here, or…? And you just think, it's more of a harassment than an enjoyment" GSI02: Patient, small site randomised to Enhanced Webpage and Email List Invitation

"We live in quite a small community here in [County] but there's several people that aren't computer literate. And I think to presume that everybody has got access to web pages and what have you would be a mistake. And also, even things like the bandwidth or whatever you call it here is dire. Sometimes our connection is awful and I still know people in [County] who can't get a connection so if they're going to have to go to Costa Coffee to get connected to find out the results of a trial, that doesn't feel very comfortable." DLI01: Patient, large site randomised to Basic Webpage, Printed Summary and Email List Invitation

One woman commented that the process of having to type in a URL from the Patient Update Information Sheet (e.g. http://bit.ly/ICON8-L11) to get to the webpage was a barrier to accessing the results, and she would have preferred to have been sent them by email without having to visit a webpage to sign up for the email list.

5.2.8.2.4 Other ways in which patients found out the ICON8 results

Some patients reported finding out the ICON8 results in ways additional to their Show RESPECT randomisation. The most common of these alternative ways of finding out the results was being told directly by their consultant, research nurse or trial administrator. While, for most of these reports, it is unclear whether the discussion was initiated by the patient or the site staff, a few patients said they had asked for the information.

Some patients at sites not randomised to the printed summary who were not regular computer users contacted site staff to request the information to be sent by post (this was explicitly included as an option in the Patient Update Information Sheet). However, not all people who experienced problems accessing the webpage did reach out to site staff for a printed copy of the results. Some patients had actively searched for the results online (as opposed to visiting the webpage included in the Patient Updated Information Sheet). One patient reported hearing about the results as part of a course on ovarian cancer, while another found out via a newspaper article.

5.2.9 What were patients' attitudes to trial participation and the ICON8 results?

5.2.9.1 Quantitative results on attitude to research

131/146 (90%) of respondents reported being willing to take part in future research, with no evidence of difference between the Show RESPECT interventions (Table 5.10). The adjusted odds ratio for Enhanced vs Basic Webpage was 0.80 (95% CI: 0.38 to 1.70, p=0.567), for Posted Printed Summary vs no Posted Printed Summary was 1.09 (95% CI: 0.52 to 2.28, p=0.827) and Email List Invitation vs no Email List Invitation was 0.70 (95% CI: 0.33 to 1.53, p=0.375).

132/147 (90%) said they were likely to recommend taking part in research to others, again with no evidence of difference between the Show RESPECT interventions (Table 5.10). The adjusted odds ratio for Enhanced vs Basic Webpage was 1.17 (95% CI: 0.56 to 2.44, p=0.671), for Posted Printed Summary vs no Posted Printed Summary was 1.23 (95% CI: 0.59 to 2.57, p=0.579) and Email List Invitation vs no Email List Invitation was 0.77 (95% CI: 0.36 to 1.65, p=0.507).

5.2.9.2 Patients' reflections on being part of a trial

Patients' reflections on being part of the ICON8 trial were overwhelmingly positive. For some, this was mainly down to the relationship with their site staff, often particularly with their research nurses. Patients talked about being glad they had taken part in the trial, despite the results not showing the improvement they had hoped for. Others talked about being grateful for being able to be part of the trial. Patients felt that their participation had been valued by their site staff. Patients did not seem to find taking part in the trial a burden. Patients' motivation for taking part in trials is discussed in Section 7.2.

> *"The experience itself has been great because my research nurses that have been dealing with it have been really helpful." DMI01: Patient, medium site*

> *"I think they went to a great deal of trouble, and I think they really are working hard at it, and it was important to them; that was quite evident, that it was important to them." GMI01: Patient, medium site*

While, for most patients, trial participation was a very positive experience, a few negative aspects did come up. Some patients found the questions about sex in the ICON8 Quality of Life questionnaire intrusive.

> *"I kind of objected to the questions on intimacy so I left those. I can see that it might have mattered to perhaps younger people, not that I'm saying it doesn't matter to me, but it felt a bit more intrusive after the first year I suppose." CLI01: Patient, large site*

Table 5.10: Outcomes relating to willingness to take part in or recommend taking part in research

	Webpage			Posted Printed Summary (PPS)			Email List			Overall
	Basic n (%)	Enhanced n (%)	Unadjusted OR (uOR)[1] (95% CI) p-value Adjusted OR (aOR)[2] (95% CI) p-value	No PPS n (%)	PPS n (%)	Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value	No Invitation n (%)	Invitation n (%)	Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value	n (%)
How willing are you to take part in future research?[3]										
Very unwilling	1 (1)	2 (3)	uOR: 0.77 (0.37 to 1.62) p=0.494 aOR: 0.80 (0.38 to 1.70) p=0.567	3 (5)	0 (0)	uOR: 1.11 (0.54 to 2.30) p=0.777 aOR: 1.09 (0.52 to 2.28) p=0.827	2 (3)	1 (1)	uOR: 0.72 (0.34 to 1.51) p=0.380 aOR: 0.70 (0.33 to 1.53) p=0.375	3 (2)
Quite unwilling	1 (1)	1 (1)		1 (2)	1 (1)		1 (1)	1 (1)		2 (1)
Not sure	6 (8)	4 (5)		2 (3)	8 (10)		3 (4)	7 (9)		10 (7)
Quite willing	9 (13)	16 (21)		13 (20)	12 (15)		10 (15)	15 (19)		25 (17)
Very willing	54 (76)	52 (69)		47 (71)	59 (74)		51 (76)	55 (70)		106 (73)
How likely are you to recommend taking part in research to others?[4]										
Very unlikely	3 (4)	3 (4)	uOR: 1.13 (0.55 to 2.31) p=0.739 aOR: 1.17 (0.56 to 2.44) p=0.671	5 (7)	1 (1)	uOR: 1.28 (0.63 to 2.62) p=0.491 aOR: 1.23 (0.59 to 2.57) p=0.579	2 (3)	4 (5)	uOR: 0.82 (0.40 to 1.69) p=0.594 aOR: 0.77 (0.36 to 1.65) p=0.507	6 (4)
Quite unlikely	1 (1)	1 (1)		0 (0)	2 (3)		1 (1)	1 (1)		2 (1)
Not sure	6 (8)	1 (1)		2 (3)	5 (6)		4 (6)	3 (4)		7 (5)
Quite likely	11 (15)	17 (23)		15 (22)	13 (16)		11 (16)	17 (21)		28 (19)
Very likely	51 (71)	53 (71)		45 (67)	59 (74)		49 (73)	55 (69)		104 (71)

[1] Adjusted for strata, randomisation phase (early vs late) and clustering

[2] Adjusted for age, education level and internet use as well as strata, randomisation phase (early vs late) and clustering

[3] For calculating the odds ratios, the very unwilling, quite unwilling and not sure were merged for this variable

[4] For calculating the odds ratios, the very unlikely, quite unlikely and not sure were merged for this variable

Some found trial participation a lonely experience, although seeing the nurses regularly gave others an opportunity to talk about their health in a way they were unable to with family and friends. One patient at a large site talked about becoming "part of the furniture" after a while, and that this affected the information she was given about her treatment and health.

> *"I suppose you can feel quite alone on the trial. I don't know anybody or I don't know the numbers that they had in [Hospital] or anything about any of the others, so I never met anybody who was on it as well." DLI01: Patient, large site*

5.3 Discussion

5.3.1 Summary of key findings

Show RESPECT found that nearly all of the women taking part in an ovarian cancer treatment trial said that they wanted to know the trial results. The opt-out Posted Printed Summary was effective at increasing patient satisfaction with how the results were communicated, and also allowed more patients who wanted to know the results to find them out. Importantly, none of the patients who did not want to know the results found them out with any of the modes of communication. A two-stage process, informing patients that the results are available and how to access them, rather than automatically sending results out to all patients, can help ensure that any patients who do not want to find out the results do not have the results forced upon them. This is especially important in trials where the patient population may be vulnerable, or the results may be emotionally challenging for some patients. The additional features of the Enhanced Webpage did not increase satisfaction with how the results were communicated compared to the Basic Webpage, but did lead to a significantly higher proportion of patients reporting that it told them everything they wanted to know. The lack of uptake of the Email List suggests that for similar trial populations it is not worth creating email lists at the end of the trial.

5.3.2 Strengths of this study

Show RESPECT employed a cluster randomised factorial design to assess three methods of sharing results with participants, allowing us to be confident that the differences observed were due to the interventions, rather than other differences between the groups. Patients in the Show RESPECT study were not aware of how the results were shared with patients from other sites. This means their responses to the quantitative questionnaire were not coloured by knowledge of interventions others had received.

I carried out extensive patient and public involvement to ensure the study was asking a question that was important to patients, and that the interventions

tested were appropriate. The interventions selected were designed to be easily replicable in other studies. The mixed methods approach allowed us to explore the reasons behind the quantitative results, while gaining an overall picture across the study population, and the 'following the thread' approach to triangulation allowed me to generate a multifaceted picture of patients' experience of finding out trial results, while using the analytical techniques appropriate for each type of data[96].

I reached inductive thematic saturation at the 13th participant interview. Inductive thematic saturation is when new themes or codes are no longer being identified within the data, and new theoretical insights are not being gained[111]. This was also the point at which 'data saturation' was reached, when new data repeat what was expressed in previous data[111]. I cannot rule out the possibility that further codes and insights may have been generated had I interviewed many more participants, but given the diminishing number of new insights over the final three interviews (with no new insights in the final interview), and the lack of new volunteers who filled the remaining gaps in my sampling frame (see Section 5.2.3) it is unlikely that interviewing more women would have substantially added to my understanding of the views and experiences of women around receiving the ICON8 results.

5.3.3 Limitations of this study

Budget constraints meant I was unable to send questionnaires to all ICON8 participants at the participating sites. However, I used random selection of participants to avoid selection bias, and the characteristics of respondents in terms of age and ICON8 arm are similar to that of all eligible participants at trial sites. The response rate of those invited to complete the questionnaire was 65%. We cannot discern if there are differences between respondents and non-respondents in other potentially relevant characteristics (e.g. education level, computer literacy), however respondents cover the range of these characteristics, and the subgroup analysis showed no evidence of heterogeneity in treatment effect by these subgroups.

5.3.4 Conclusion

Understanding the perspectives of trial participants is vital to working out how best to share trial results with them. The results described in this chapter suggest that using opt-out Posted Printed Summaries may improve satisfaction with how the results are shared, and increase access to results, compared to webpages alone, in trials with similar patient populations and trial settings. However, sending printed summaries by post has resource implications for sites. Understanding the perspectives of site staff is also essential if we are to

improve practice in this area for trials where communication with participants is led by sites. The next chapter explores the quantitative and qualitative findings from the site staff data gathered in Show RESPECT.

6. Site staff perspectives on the benefits, feasibility and resources needed to share the ICON8 results with participants

6.1 Overview of the scope of this chapter

This chapter presents qualitative and quantitative results from the site staff data from Show RESPECT, including the characteristics of site staff who took part in the study, their views on sharing results with participants and the processes used in Show RESPECT. It explores the resource implications of the Show RESPECT interventions for both sites and the Clinical Trials Unit (CTU), including staff time and other costs. Quantitative and qualitative data that relate to the same topic are presented alongside each other, using a 'following the thread' triangulation approach (see Section 3.2.5). Quotes from site staff are shown in indented, purple italic text. This chapter concludes with a short discussion of these results, including key findings, strengths and limitations.

Chapter 8 brings together the views of site staff and patients on the information contained within the summaries, and the information products used to convey the results in Show RESPECT. Chapter 9 explores site staff and patients' views on other factors that influence patient satisfaction with how trial results are shared.

6.2 Recruitment and characteristics of site staff respondents

In total, 68 staff from 41 sites returned at least one Case Report From (CRF). No CRFs were received from 2/43 of the randomised sites due to staff turnover. Both these sites were randomised to the Basic Webpage, No Printed Summary and Email List Invitation. Figure 6.1 shows the CONSORT diagram for site staff questionnaire respondents, and the number of sites where no responses were received for either of the two site staff questionnaires (CRF2, which asked about time spent posting documents, and CRF3 which asked about time spent dealing with queries), by each of the 8 combinations of interventions. We received no CRF2 from 5 sites, and no CRF3 from 7 sites (only sites that received queries from participants were expected to complete CRF3). Table 6.1 shows the numbers of sites and questionnaires received by margin (i.e. the three factorial randomisations). Sites that we received no CRF2s from were mostly allocated to the Basic Webpage and No Posted Printed Summary. Sites that we received no CRF3s from were split between the randomisations.

Chapter 6 Summary Box

Why was this study done?

- For many trials, Sponsors are reliant on site staff to share results with participants, so understanding their views on this topic is important
- Lack of resources or time can be a barrier to sharing results with participants, so it is important that approaches are feasible for site and CTU staff to implement
- Data on costs and time requirements of different approaches to sharing results could help future trials budget and plan appropriately

What did I do?

- I collected quantitative and qualitative data from site staff involved in sharing results with participants at Show RESPECT sites, covering their views on sharing results with participants, their experience of sharing the ICON8 results, and the resources required to implement the Show RESPECT interventions
- I also collected data on the time and costs to the CTU for developing, reviewing and disseminating the Show RESPECT interventions

What did I find out?

- Site staff were strongly supportive of sharing results with participants, citing benefits including it being a way of showing that participants' contribution to trials are respected and valued, repaying trust, giving something back to participants, increasing awareness of the importance of research, and helping participants process their trial experience
- Site staff felt that the process of sharing results with patients in Show RESPECT was generally straight-forward and not too time-consuming, although the time required was more of a challenge for some staff at sites with large numbers of participants
- Sharing results via a posted printed summary increased costs to sites by around £14 per participant compared to no posted printed summary
- The email list intervention was the most time-consuming for CTU staff, which accounted for a third of the hours spent on developing, reviewing and disseminating the Show RESPECT interventions

Chapter 6 Summary Box ctd.

What do these findings mean?

- These findings show that all of the approaches adopted in Show RESPECT (Patient Update Information Sheet with links to Basic and Enhanced Webpages and Email List; Posted Printed Summary) were feasible for staff at the participating NHS hospitals to implement, acceptable to those staff, and could potentially be adopted by other studies in similar settings
- Trials with sites that have very large numbers of participants will need to consider how to support these sites with sharing results with participants
- The time and costs of sharing results with participants are small in comparison with the overall costs of trials, and time required for other trial processes
- The estimates of costs and time required can be used to inform planning and budgeting of future trials

Most respondents were in nursing (63%) (e.g. research nurse) or administrative (30%) (e.g. trial coordinator) roles, with only five clinicians returning questionnaires. There was a wide range of years of experience working in trials among respondents, with more than a quarter having worked on trials for more than 10 years, while 13% had been working on trials for less than a year. Respondents generally worked on many trials, with 72% working on more than 10 at the time they completed the questionnaire. Two thirds spent almost no time each week working on ICON8, reflecting that many of the participants are no longer in follow-up, and visits are now infrequent. Around half of respondents had been working on ICON8 for two years or less, while 38% had been working on the trial for more than 5 years. 81% of respondents had been involved in sending information by post, and 63% had been involved in answering patient queries about the results. These data are shown in Table 6.2.

For the qualitative study, I interviewed 11 site staff from 12 sites. I was able to recruit at least the target number of interviewees in all parts of the sampling frame. Table 6.3 shows the characteristics of site staff who were interviewed. They covered the range of site strata, job roles, and were evenly split between sites randomised to No Posted Printed Summaries vs Posted Printed Summaries, giving me a range of perspectives.

Figure 6.1: CONSORT diagram for site staff

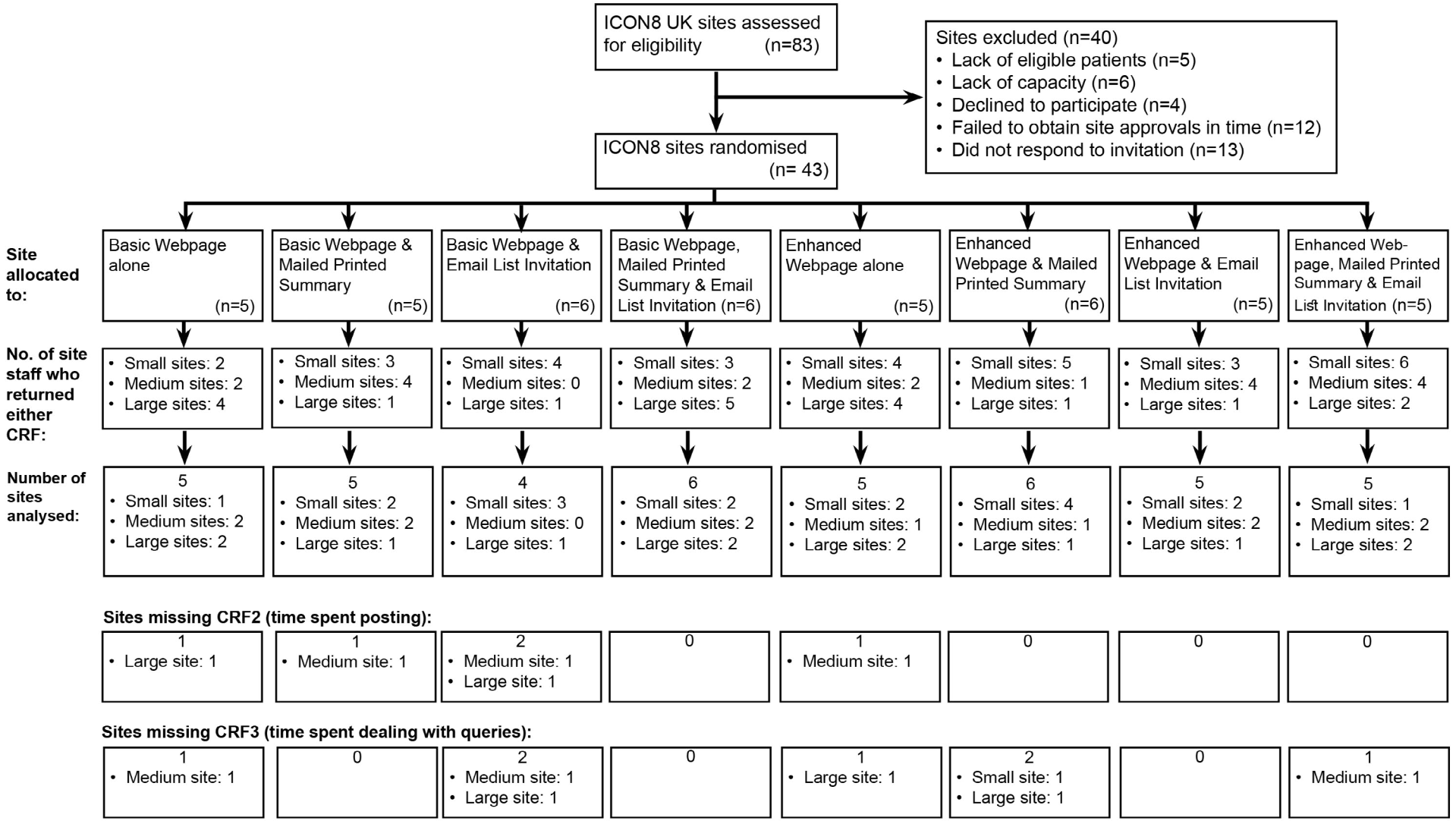


Table 6.1: Recruitment of sites and site staff respondents

	Overall	Webpage		Posted printed summary		Email list	
		Basic webpage	Enhanced webpage	No printed summary	Printed summary	No invitation	Invitation
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of sites							
TOTAL	43 (100)	22	21	21	22	21	22
Small sites	17 (40)	8 (36)	9 (43)	8 (38)	9 (41)	9 (43)	8 (36)
Medium sites	13 (30)	7 (32)	6 (29)	6 (29)	7 (32)	6 (29)	7 (32)
Large sites	13 (30)	7 (32)	6 (29)	7 (33)	6 (27)	6 (29)	7 (32)
Number of site staff who returned either CRF							
TOTAL	68	35	33	33	35	35	33
Small sites	28 (41)	14 (40)	14 (42)	13 (39)	15 (43)	14 (40)	14 (42)
Medium sites	19 (28)	8 (23)	11 (33)	8 (24)	11 (31)	9 (26)	10 (30)
Large sites	21 (31)	13 (37)	8 (24)	12 (36)	9 (26)	12 (34)	9 (27)
Number of sites missing both CRFs (as % of sites)							
TOTAL	2 (5)	2 (9)	0 (0)	2 (10)	0 (0)	0 (0)	2 (9)
Small sites	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Medium sites	1 (8)	1 (14)	0 (0)	1 (17)	0 (0)	0 (0)	1 (14)
Large sites	1 (8)	1 (14)	0 (0)	1 (14)	0 (0)	0 (0)	1 (14)

Table 6.2: Site staff questionnaire respondent characteristics

	Overall	Webpage		Posted printed summary		Email list	
		Basic webpage	Enhanced webpage	No printed summary	Printed summary	No invitation	Invitation
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Job role							
Medical	5 (7)	3 (9)	2 (6)	3 (9)	2 (6)	3 (9)	2 (6)
Nursing	42 (63)	23 (66)	19 (59)	22 (69)	20 (57)	23 (66)	19 (59)
Administrative	20 (30)	9 (26)	11 (34)	7 (22)	13 (37)	9 (26)	11 (34)
Years of experience working in trials							
Less than 1 year	9 (13)	4 (11)	5 (15)	4 (12)	5 (14)	4 (11)	5 (15)
1 - 5 years	24 (35)	11 (31)	13 (39)	14 (42)	10 (29)	12 (34)	12 (36)
6 - 10 years	16 (24)	9 (26)	7 (21)	6 (18)	10 (29)	9 (26)	7 (21)
More than 10 years	19 (28)	11 (31)	8 (24)	9 (27)	10 (29)	10 (39)	9 (27)
Number of trials they currently work on							
1-5	7 (10)	5 (14)	2 (6)	3 (9)	4 (11)	3 (9)	4 (12)
6-10	12 (18)	6 (17)	6 (18)	7 (21)	5 (14)	4 (11)	8 (24)
More than 10	49 (72)	24 (69)	25 (76)	23 (70)	26 (74)	28 (80)	21 (64)
Time they currently spend working on ICON8							
Almost none	45 (67)	21 (62)	24 (73)	21 (66)	24 (69)	19 (56)	26 (79)
Around one day per week	21 (31)	13 (38)	8 (24)	10 (31)	11 (31)	14 (41)	7 (21)
Around two days per week	1 (1)	0 (0)	1 (3)	1 (3)	0 (0)	1 (3)	0 (0)

	Overall	Webpage		Posted printed summary		Email list	
		Basic webpage	Enhanced webpage	No printed summary	Printed summary	No invitation	Invitation
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of years they have worked on ICON8							
Less than 1 year	16 (24)	6 (17)	10 (30)	9 (27)	7 (20)	6 (17)	10 (30)
1-2 years	17 (25)	10 (29)	7 (21)	12 (36)	5 (14)	12 (34)	5 (15)
3-4 years	9 (13)	3 (9)	6 (18)	5 (15)	4 (11)	5 (14)	4 (12)
5 years or more	26 (38)	16 (46)	10 (30)	7 (21)	19 (54)	12 (34)	14 (42)
Involvement in sharing the ICON8 results							
Sending information by post	55 (81)	26 (74)	29 (88)	28 (85)	27 (77)	31 (89)	24 (73)
Answering patient queries	43 (63)	24 (69)	19 (58)	23 (70)	20 (57)	18 (51)	25 (76)
Other	7 (10)	3 (9)	4 (12)	3 (9)	4 (11)	2 (6)	5 (15)

Table 6.3: Characteristics of site staff interviewed for the qualitative study

Characteristics	No. of interviewees
Total interviewed	11
Show RESPECT randomisation*	
Works at site randomised to posted printed summaries	6
Works at site not randomised to posted printed summaries	6
Site strata (based on number of ICON8 participants)*	
Small	2
Medium	5
Large	5
Staff job role	
Medical	2
Nursing	5
Administrative	4

* One interviewee worked at two sites of different sizes, randomised differently

6.3 Site staff's access to and experience of sharing previous trial results

Most of the site staff I interviewed worked on many trials at any one time, and some of them had long experience working on trials, often across several disease areas. However, for many of them, ICON8 was the first trial for which they had been asked to systematically share the results with trial participants.

6.3.1 Site staff's access to study results

Site staff said they generally found out the results of studies they had worked on, usually via email or newsletter from the Chief Investigator, Sponsor or trial coordinator / Contract Research Organisation just before the results are made public, or sometimes through it being fed back from clinicians in their team. Access to results may be better for Principal Investigators at sites than for other members of the team involved in delivering the study.

> *"I think more studies now are beginning to let us know… so I'll get a summary and more studies are beginning to let patients know as well, so I think it has improved, probably… this is off the top of my head but probably within about the last five years or so. Before that, I don't think you ever got to know the outcomes and we've been quite keen to try to feed study outcomes back to the teams that have actually been helping with the studies as well, and that's been quite hard because it's really hard to find." DMRNI02: Research Nurse, medium strata site*

6.3.2 Experience of sharing trial results with participants in other trials

For most of the site staff I interviewed, most of their previous experience of sharing results with participants has been in an ad hoc way, when patients

come back to clinic and ask about the results. For some site staff (even those with considerable trial experience), Show RESPECT was the first time they had been asked to offer results to all participants. For others, the picture varied, with some trials sharing results, and others not providing information to feedback to participants.

> *IV: Is sharing overall trial results with participants something that you do routinely?*
>
> *HLCLI02: "I think we have to say it isn't. It would normally be something we would do on an ad hoc basis when we see patients in clinic, who either enquire about the results... Or, when those results are fresh in our minds and we remember that particular patient participated in that study." HLCLI02: Clinician, large site*

A few did talk about having shared results with participants systematically in previous studies. This was usually done through passing on letters or newsletters to participants, either through the post or at their next clinic visit, if they are still in follow-up. Sometimes instead of giving printed information, the information may be relayed verbally.

> *"We don't always get that information to pass forward to patients and participants. But if we do it's usually to be honest in the form of newsletters, especially thinking of quite a few breast trials that I worked on." AMRNI05: Research Nurse, medium site*

The staff member who was responsible for sharing results varied, with some clinicians wanting to share the results, while in other cases it has been the research nurse, or a combination of the two. The level of information that is shared may be tailored according to the site staff's perception of patients' level of interest and understanding.

> *"I treat each patient as an individual. Some patients who struggle with information, sometimes they don't want to know some of the results. Some of them do and so I would treat each patient as an individual and give them the results accordingly. Sometimes the results will be vaguer than is specified in the publication, so I give them an approximation rather than say this definitely such and such percentage. Some people may take a small risk, a medium risk or a high risk of recurrence and some patients prefer it that way. So, I do have to be flexible with giving results." EBLMCLI02: Clinician, large and medium sites*

Where site staff have shared results with participants in the past, their impressions were that participants wanted to know the results, but did not come back with lots of questions. Site staff thought that participants in previous studies who had been informed of the results reacted positively.

> *"Generally they've been interested and quite enthusiastic to hear about the outcomes of the study. It's very unusual for us to get any negative comments back in that circumstance." HLCLI02: Clinician, large strata site*

6.3.3 Support from trials units to share results in other trials

Generally, site staff said they had not received much support from the trial units responsible for coordinating trials in terms of sharing results with participants for previous studies. At best they have been provided with the information and asked to give it out. Some interviewees thought that support from trials units for sharing results with participants may be increasing, with the issue being discussed as part of the consent process, but this still is not common. Clinical trials units could provide further support to sites around sharing results through providing clear patient-facing information, and training.

> *"I think it might be reasonable when we get more experience with doing this, of having specific training, to allow maybe research nurses or clinicians at very trial-active sites to discuss experience, and maybe communication strategies for dealing with those difficult scenarios. We've all got techniques that we use for the difficult consultations that we have, unfortunately, very regularly in oncology. It's a question of working out how we can apply those to this particular setting." HLCLI02: Clinician, large site*

6.4 Site staff views on sharing results with trial participants

Site staff who were interviewed were overwhelmingly positive about sharing results with participants, describing it as "necessary", "a good thing", "right", "brilliant", "an excellent idea", "the way forward" and "courteous". They talked about participants being "entitled to know". One research nurse talked about it being, in principle, like sharing test results, which is standard practice.

> *"I think it should be a priority" CSRNI01: Research Nurse, small site*

6.4.1 What motivates site staff to share trial results with participants?

When talking about what motivated them to share trial results with participants, site staff linked this back to the reasons to do the trial in the first place, both from a trialists' perspective and a participants' perspective. They argued that, from a trialists' perspective, the reason to do trials is to find out the results, and that therefore communicating those results is important. They believed that patients often agree to take part in trials because they want to improve treatment for others, and so communicating results and implications of those results helps them to see how that aim has been met and provides closure.

> *"The reason why I can imagine patients went on the trial in the first place is, one, because they obviously wanted to get more care, but also, it's just helping people out in the long run. So if they see the fruits of their labour as it were, yes, it would be a really good thing for them." GMTCI02: Trial Coordinator, medium site*

6.4.2 Views of site staff around the benefits of sharing results with participants

6.4.2.1 Sharing results as a way of showing respect and valuing participants' contribution

The most frequently mentioned benefits of sharing trial results related to the relationship with participants, repaying participants' trust and contribution to the trial, giving something back to participants, showing they are valued and respected, and not treating them like guinea pigs. There was recognition that trial participation often involves risk or inconvenience, and a feeling that sharing results was a way of repaying that, in part. Several site staff talked about sharing results as being a way of involving and empowering participants.

> *"They've given their time and effort to take part in the study and I think, you know, it's kind of courteous, isn't it, just to let them know actually what impact, or even if it hasn't had an impact, but still what outlines so that they've got a record of their contribution." GSTCI03: Trial Coordinator, small site*

6.4.2.2 Sharing results to increase awareness of the benefit of research

Site staff also talked about the knock-on benefits of sharing results with participants, increasing knowledge of the benefits or impact of research, which they may then talk to others about (such as friends and family who have supported them through the trial process), and potentially increasing the likelihood of people agreeing to take part in future research. This was particularly the case where the trial had a 'positive' result, but site staff thought that it was also important to be transparent where trials hadn't found what they were hoping to.

> *"So they will talk about it in the sense of 'I went on this trial, and they've done this, or they've told me that' and 'oh, you should go on this trial because your care, your treatment, your aftercare…', it, it makes it a more positive experience." CSRNI01: Research Nurse, small site*

6.4.2.3 Sharing results to help participants process their trial experience

Another perceived benefit of sharing results with participants was that it would help participants understand the effort that had gone into the study and reinforce that they had been given high quality care (even if they were randomised to the control arm). It also provides an opportunity for participants to reflect on their own trial experience and discuss it with their study doctor.

> *"An opportunity to discuss the trial, and any outstanding questions that they may have in relation to that. But also, revisit the rest of their ovarian cancer journey." HLCLI02: Clinician, large site*

6.4.3 What inhibits site staff from sharing trial results with participants?

Providers talked about two types of concerns regarding sharing trial results with participants: concern around the emotional impact of the results for participants, and concern around the practicalities of sharing the results. The emotional impact may depend on the study whose results are being communicated, what it found, how those results are presented, and which arm the participant was in. The emotional impact may also depend on the participants' health at the time they receive results.

> *"It may differ when the results are available, they may be at a much more difficult time during their illness. Their cancer could have recurred. They could be in a situation where they're getting close to the end of life and very much in the palliative phase of their illness. Sharing information at that point of time could potentially be upsetting for them. It may, particularly if it was found that they were on a treatment that was less effective, means that they will ask questions about… What if? There may be a risk of causing some emotional distress to a small proportion of participants." HLCLI02: Clinician, large site*

If the trial had 'negative' results, or if participants were not in the arm that did best, there is the danger that sharing results with participants could lead to negative feelings about research, or distress, and that participants may talk about trials negatively to others. Careful wording of the results is needed in this case to ensure participants understand that benefit to science of the research, even if it will not lead to a change in practice.

> *"Say if you were on an arm which is very inferior to the treatment which was already there, you have got to find ways of how you can impart this information to these participants without upsetting them." BMRNI04: Research Nurse, medium site*

The clinicians I spoke to expressed the need for care in how sharing results is done, to ensure participants are not unnecessarily distressed or confused. Patient and public involvement in the preparation of information about results for participants was identified as a way of mitigating the risk of causing upset. Having information carefully prepared and written specifically for patients was seen as a better way of managing the process than the current ad hoc approach, which depends on participants asking clinicians, and clinicians remembering the key findings when asked.

> *"We do have a duty to give the patient information, it's just being wise and careful to give that information well, in a way that patients can understand. So, yes, we have a duty to give it it's just how we give it and how much of it we give it. And like any information we have to time that well and be sensible about who we're giving that to." EBLMCLI02: Clinician, large and medium sites*

6.4.4 Providers' perception of the views of colleagues around sharing results

The site staff I interviewed felt that their colleagues were also supportive of the principle of sharing results with trial participants.

> *"At the end of the day, we all work really hard to deliver cancer research, to coordinate trials, and the sole purpose of it is to, you know find an outcome, find a result, and a hoped for result, so yeah, I think we would all share the same thought on that, yeah." FLTC01: Trial Coordinator, large site*

One clinician talked about clinicians being more likely to support sharing results with participants when the results are 'good'. Another clinician suggested that colleagues in less research active sites might find sharing results more difficult.

> *IV: Do you think generally, your views around it, it being a good idea to share results generally with participants, do you think those are shared by your colleagues?*
>
> *HLCLI02: "I think it probably would be for the majority of colleagues. I'm coming at it from a slightly biased perspective, being a very trial-active clinician. And so, somebody who does really value the extra sacrifice in terms of time etc, that my patients put in, to taking part in clinical trials. I think it may be in some settings, if people have got fewer patients on trials, they might find that a little bit more difficult to share those results without support. So, they may have more reservations about taking this forward routinely." HLCLI02: Clinician, large site*

6.4.5 Who do site staff think should be responsible for sharing results with participants?

There were differing views around who should be responsible for sharing results with participants. The most common view was that it should come from the site that had been looking after the patient, rather than the trial Sponsor. Reasons for this include that it is the site rather than the Sponsor that has the relationship with the participant, and is in a position to support the participant, and that the logistics of the Sponsor sending out the results would be impractical. Conversely, a research nurse at a site that had a large number of participants in trials was concerned that, if instituted for all trials, this would be extremely time-consuming for site staff, and said it would be better for the results to go directly from Sponsors to the participants.

> *"I think it's probably a responsibility for us as investigators to, when we've got patients who are keen to participate in trials, to be open and keep them informed in terms of the outcomes of the studies that they have been participating in, if they want to be informed about that." HLCLI02: Clinician, large site*
>
> *"The only problem with our site is we recruit so many patients onto our trials, it would be extremely time consuming. Now whether we could, you know, whether the Sponsors could send something out directly to*

the patients themselves, you know, with an option to receive the results or not. That would probably be a better option, you know, I don't know. Again, it's just the volume of patients that we've got on trial here. So, it's a, you know, it's a lot of information to send out to people, you know, when we've got so many patients on trial." HLRNI03: Research Nurse, large site

6.4.6 Which trials should share results with participants?

Most interviewees felt that all trials that consent participants should offer results to participants, as part of the routine process of the trial. No interviewees were able to think of a scenario which would make it inappropriate to share results with participants, however, what the results show may affect how the results should be shared, with additional support or more individualised approaches potentially being needed in some scenarios. One clinician who was interviewed identified circumstances when it may not be appropriate to share results routinely, such as trials in emergency settings where the patient did not give consent to participate. Most site staff recognised that not all participants will want to know the results, so an opt-in or opt-out process will be needed to ensure that people who do not want the results are not exposed to them (see Section 8.6).

"There may be certain circumstances where you are doing trials in other situations, maybe in emergency settings, where you're not gaining patient consent. It might be inappropriate to share trial results routinely at that point. But in oncology I think it's beholden on us to do that." (HLCLI02: Clinician, large strata site)

6.4.7 When should trial results be shared?

There is often a substantial gap between when trial teams first know the results (internally), when they are first presented at a scientific conference, and when they are published in a peer reviewed journal. Media coverage may take place around presentation or publication of the results, or not at all. The question of when, during this often lengthy process, the results should be shared with participants is difficult. Some site staff felt it should be done as soon as the team are sure of what the results were. Some were keen that participants were informed prior to the results being reported by the media, as finding out the results via the media would not be good. Where the media may cover results at the time of presentation, then the results may need to be communicated to participants first or concurrently.

"If they were to find out that way via press coverage because you haven't let them know that it's going to be coming out in the public domain, then that might annoy certain individuals. You probably wouldn't want to find out, like, put ITV on, the news has come out, and then all of a sudden the paparazzi are there talking about this trial. You'd probably be sitting there thinking, I could've done with this information earlier, couldn't I?...

Out of respect for the patient really, you should be telling them as early as possible, I can imagine." GMTCI02: Trial Coordinator, medium site

Waiting for publication of the results, which may often be months or even a year, was seen by some as being too long, particularly for a condition like ovarian cancer when some patients may not be alive at the later point to find out the results.

"As long as you are confident that is what is going to be written in the journal. You are sending this information to people who participated in the study. I think it's better to let them know as soon as you are confident about whatever has been outlined. Like, waiting for a year, they might be dead." BMRNI04: Research Nurse, medium site

For most, the period between presentation and publication of the results was seen as the best option, as researchers will have had some feedback and discussion around the results, but not delaying the communication to participants unnecessarily.

"I suppose my thought is that it probably would be okay to share that after the presentation, rather than waiting for it to go to a journal and go through the peer review process. Because that in itself will often add another twelve months or even longer to the timeline and that's taking you even further out from the time the patients were actually participating in trial. I think doing that once the results are presented, and you've had some initial feedback from the discussions that happen at the conference would be the right time to do that. So, in a sense, it's a question of preparing that information in parallel with the research presentation, isn't it? Being in a position shortly after the conference to be able to take forward the dissemination to study participants." HLCLI02: Clinician, large site

6.5 Site staff experience of sharing the ICON8 results

6.5.1 The process of sharing results

Site staff described several stages to sharing results with participants, from preparing participants to receive results, checking participants' health, finding addresses, sending the Patient Update Information Sheet, then, if randomised to it, sending the Printed Summary, before providing further follow-up and support. The process of sharing results as set out in the Show RESPECT protocol is described in Section 4.6.

6.5.1.1 Preparing participants to receive the trial results

In Show RESPECT, the protocol specified that a Patient Update Information Sheet should be sent to all participants. For those randomised to no printed summary, this gave details of how the results could be accessed (via website, email, or asking site staff for a printed copy of the results). For those

randomised to the posted printed summary, this explained that a printed summary would be posted to them in three weeks time, unless they informed staff they did not want to know the results (opted out). It also included a reminder of what the trial was looking at, and how it was done.

The concept of preparing participants to receive results came up repeatedly in both interviews and questionnaires from site staff. Some thought that this should start at the point patients join the trial.

> *"Right at the very beginning, we should be telling them, when there is an update, we will be letting you know." CSRNI01: Research Nurse, small site*

The importance of preparing participants to receive results stemmed partly from recognition that not all participants would want to know the results, and so it was important to offer them the opportunity to opt in or out of receiving them. Some site staff framed this as seeking consent to receive results. Views differed on the timepoint at which that consent should be sought, with some site staff saying this should be done at the start, when participants are joining the trial. This was being done in some trials that site staff were working on. However, some site staff thought patients might change their minds between joining the trial and the results becoming available, meaning that they would have to be re-consented nearer the time, or that consent should only be asked for when the results are actually available.

> *"I think it would be a really good idea going forward to, you know, ask patients if they want the results when consenting to the clinical trial, And, again, ask them once they've completed the treatment if they'd still like to receive the results." HLRNI03: Research Nurse, large site*

The other driver behind discussion of the need to prepare participants prior to sharing results was that results may potentially be upsetting, depending on what the trial found, and the arm the patient had been randomised to.

> *"I think if you put it on the update sheet that there was… not saying which particular arm was the best, but just saying that they should be prepared for some sort of news that they may not find good. I don't know, but just preparing them beforehand might or would help if that were the case." CLTCI04: Trial Coordinator, large site*

While, in Show RESPECT, the Patient Update Information Sheet was designed as a way of preparing participants to receive results (and giving them the opportunity to opt out/in, depending on what interventions their site was randomised to), some site staff added a preliminary step to prepare participants to receive the Patient Update Information Sheet through telephoning them or talking to them in clinic to let them know it was coming. However, not all site staff agreed that this step was needed or a good idea.

> *"We sent the information sheets out, then contacted them and let them know they're coming. I'm pretty sure, obviously, I wasn't privy to every*

conversation that [research nurse] had, but she talked them through it. That's a really good way of doing it because if that had just ended up on their doorstep, they'd have read it and then just probably thrown it in the bin because it didn't come with any compliment slip or they didn't really know what it was." GMTCI02: Trial Coordinator, medium site

"I don't agree with phoning the patients, just because, you know, a lot of our patients, you know, are busy with day-to-day life and it's not, I don't think it's nice just calling them and reminding them of it all" FLTCI01: Trial Coordinator, large site

6.5.1.2 Checking participants' health

Prior to sending out information by post, site staff checked that participants were still alive, and not too ill to receive the results. This was generally done by checking the hospital database, which was straightforward. If it required checking with the participants' GPs, that was more time-consuming.

"We have access to the database. We have access to make sure they're still alive when we're doing it. So, you've got all of that in front of you. So that side of it for us is not a problem at all." CSRNI01: Research Nurse, small site

AMRNI05: "I think all GPs wanted a letter sent before they would even say whether or not..."

IV Whether the patient was alive or not?

AMRNI05: "Yes. So that, yes, it totally depends on the GP at all whether you need to do that or not. And then they might not answer for a couple of weeks, so that can slow it down." AMRNI05: Research Nurse, medium site

6.5.1.3 Finding addresses

Finding the contact details for most participants was straightforward for site staff. However, for site staff at sites which had many participants, this process could be more time-consuming.

"I think the only thing that's slightly time-consuming is, you know, finding the address and writing the address and everything down. But in comparison to a lot of our other trials, and the work that it involves, it's not a lot of time." FLTCI01: Trial Coordinator, large site

6.5.1.4 Sending out the Patient Update Information Sheet

The Patient Update Information Sheet was seen by site staff as an important part of the process of sharing results with participants, except if results were shared during a clinic visit. Site staff were asked to keep a record of which participants had been sent the Patient Update Information Sheet, and the reasons for not sending them to any patients who weren't sent one. Some site staff included covering notes, compliments slips or letters with the Patient Update Information Sheet. This is discussed in Section 8.5.

6.5.1.5 Leaving time between the stages of sharing results

Sites were asked to leave three weeks between sending out the Patient Update Information Sheet and the Printed Summary (if sites had been randomised to that), in order to give participants time to opt out of the printed summary. Some felt this gap was about right, whereas others felt the gap was too long.

> *BMRNI04: "Though I thought the interval between them getting the summary, because they were saying, I haven't received what you said you were going to be following up with. And I said, I don't have it, I'm waiting for it from the centre."*
>
> *IV: They were impatient?*
>
> *BMRNI04: "Yes, they were impatient because now you know they are in the enthusiasm of saying, what is actually written in there? I now want to see it and when is it coming?" BMRNI04: Research Nurse, medium site*
>
> *"I actually think giving them shorter time is probably better because I think they just forget otherwise. Yes, I think three weeks is fine, shorter probably reasonable." CLTCI04: Trial Coordinator, large site*

6.5.1.6 Sending out Printed Summaries

The process of sending out the Printed Summaries was the same as that for sending out the Patient Update Information Sheet (Section 6.5.1.4). At sites not randomised to the Printed Summary, the Patient Update Information Sheet informed participants they could request a Printed Summary from their site, which happened in some cases.

> *"I know we had the option of then sending out the printed summary. So that worked well and I think we did end up doing that for one of the patients" GSTCI03: Trial Coordinator, small site*

6.5.1.7 Further follow-up and support

There was recognition that some participants may need further support or have questions about the results. Some site staff phoned participants after they sent the Patient Update Information Sheet or Printed Summary, depending on their randomised arm, to see if participants had any questions or needed further support. Others included a note with the results saying to contact them if the participant had any questions.

> *"That was the thing, I think, we were slightly concerned about was, well, what if that raises questions, which again is why we put that you know, compliments slip in… you know, do phone us if you've got any issues with it or queries or anything." DMRNI02: Research Nurse, medium site*

6.5.2 Concerns and challenges

Most site staff (88%) reported no concerns about how they shared the ICON8 results with participants, with no significant differences between the

intervention arms. Similarly, around three quarters of site staff reported not finding anything challenging about sharing the ICON8 results, again with no evidence of differences between the arms. These figures are shown in Table 6.4.

As discussed in Section 6.4.3, some of the concerns site staff reported were around the emotional impact of sharing results. In relation to the ICON8 results specifically, some site staff were uncomfortable with sharing information on average progression free survival times, while others were concerned that participants who felt they had benefited from trial participation may be upset to learn that the trial did not find a benefit overall. The practical concerns site staff expressed included how to deal with questions the results raise for participants.

One of the main challenges identified by site staff was the time needed to share results via posted information (the Patient Update Information Sheet and Printed Summary). This was particularly an issue for staff at sites with larger numbers of ICON8 participants. Sites taking part in Show RESPECT had between 1-52 eligible ICON8 participants. Staff at smaller sites also recognised that, though it may not have been a problem for them in this study, it would be challenging in studies where there are many patients at a site. For some site staff finding addresses was time-consuming, whereas for others the need to request patients' notes in order to file copies of the results summaries was time-consuming and meant the task had to be spread over several days. Section 6.6.2 contains details of the amount of time staff reported spending on sharing the results, per participant.

> *"Finding each patient address was time-consuming." GLTCQ01: Trial Coordinator, large site*

In Show RESPECT we specified a time-period in which we wanted the results sent out to participants at each site. This timeline was felt to be too tight by some, as it meant they were unable to wait until the patients' next scheduled visits to give out the Patient Update Information Sheet. Giving sites more flexibility with when they share the results would have addressed this concern.

One challenge that came up repeatedly was patients saying they had not received information that had been posted to them.

> *"Well, the only difficulty was that they didn't receive it because it was Christmas. I think three out of the five letters didn't get there to start with, so they had to be sent again." AMRNI05: Research Nurse, medium site*

The issue of who to send the results to raised some questions for site staff. If site staff had not had contact with a patient for a while, and were aware the patient was unwell, this did raise some questions for sites over whether they

Table 6.4: Proportion of site staff reporting concerns or challenges around how the ICON8 results were shared

	Overall n (%)	Webpage: Basic n (%)	Webpage: Enhanced n (%)	Webpage: Odds ratio (95% CI) p-value	Posted Printed Summary (PPS): No PPS n (%)	Posted Printed Summary (PPS): PPS n (%)	Posted Printed Summary (PPS): Odds ratio (95% CI) p-value	Email List: No Invitation n (%)	Email List: Invitation n (%)	Email List: Odds ratio (95% CI) p-value
Any concerns about how you shared the results?										
Yes	8 (12)	5 (14)	3 (9)	0.71 (0.14 to 3.58) 0.679	2 (6)	6 (17)	2.59 (0.45 to 14.83) 0.284	2 (6)	6 (18)	3.15 (0.56 to 17.59) 0.191
No	60 (88)	30 (86)	30 (91)		31 (94)	29 (83)		33 (94)	27 (82)	
Did you find anything challenging about sharing the results?										
No	52 (76)	30 (86)	22 (67)	5.94 (0.80 to 44.27) 0.082	27 (82)	25 (71)	3.31 (0.47 to 23.52) 0.231	29 (83)	23 (70)	2.57 (0.40 to 16.59) 0.321
Yes	16 (24)	5 (14)	11 (33)		6 (18)	10 (29)		6 (17)	10 (30)	

should send the results. Similarly, if patients had transferred from one site to another, it could cause confusion over who was responsible for sharing results with that patient.

> *"There were a couple of patients who we hadn't seen for a while and knowing how appropriate it was to send the information or any of it out really, and there was one that I did send the information to who I knew was a little bit poorly but I also knew had been really keen on ICON8, so I felt okay to send it to her." DMRNI02: Research Nurse, medium site*

For some site staff, giving information out remotely, rather than face to face, was challenging as they could not gauge the reaction of patients.

One clinician identified that, in large trials with many sites, there may be challenges for trial teams getting sites to engage in sharing results with participants, due to insufficient staffing.

> *"Although the majority of sites would actively engage, there may be some sites who feel that it's an optional extra. And they don't have the staffing, and the information then doesn't get out to the participants who would actually like to have that information." HLCLI02: Clinician, large site*

6.5.3 Dealing with queries from participants

Just over a quarter of site staff reported that no participants contacted them with queries, while almost 60% were only contacted by one or two participants. No respondents reported being contacted by more than five participants. There was no evidence of significant differences between the randomised arms in the number of queries received from participants. 83% of site staff felt it was quite or very easy to deal with the queries participants raised, again with no evidence of differences between the arms. These data are shown in Table 6.5.

6.5.4 Site staff views on sharing results in future trials

Three quarters of site staff respondents said they thought the way they had shared results with participants in Show RESPECT should be the standard approach for other trials, with no evidence of differences between the randomised arms. Similarly, 79% said they would not do anything different for future trials (Table 6.6). Site staff preferences around the method used to communicate results to participants, and the reasons for these preferences, are discussed in Section 8.4.3.

6.5.5 Site staff views on the process of sharing results

Aside from the concerns and challenges described in Section 6.5.2, site staff described their experience of the process in positive terms, as "easy", "not

Table 6.5: Site staff data on dealing with queries from participants

	Overall	Webpage			Posted Printed Summary (PPS)			Email List		
		Basic	Enhanced	Odds ratio (95% CI)	No PPS	PPS	Odds ratio (95% CI)	No Invitation	Invitation	Odds ratio (95% CI)
	n (%)	n (%)	n (%)	p-value	n (%)	n (%)	p-value	n (%)	n (%)	p-value
How many participants contacted you with queries?[1]										
0	11 (27)	4 (17)	7 (39)	4.80	3 (16)	8 (36)	0.76	2 (13)	9 (36)	1.23
1-2	24 (59)	17 (74)	7 (39)	(0.53 -43.13)	12 (63)	12 (55)	(0.07 – 8.33)	11 (69)	13 (52)	(0.14 – 10.14)
3-5	6 (15)	2 (9)	4 (22)	0.161	4 (21)	2 (9)	0.824	3 (19)	3 (12)	0.851
How able did you feel to help with queries?[1,2]										
Very difficult	0 (0)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
Quite difficult	1 (3)	0 (0)	1(8)	0.27	1 (6)	0 (0)	2.61	0 (0)	1 (6)	0.75
Not sure	4 (13)	2 (11)	2 (17)	(0.02 – 3.56)	3 (18)	1 (7)	(0.24 – 28.40)	0 (0)	4 (22)	(0.08 – 7.32)
Quite easy	15 (48)	9 (47)	6 (50)	0.317	9 (53)	6 (43)	0.432	9 (69)	6 (33)	0.802
Very easy	11 (35)	8 (42)	3 (25)		4 (24)	7 (50)		4 (31)	7 (39)	

[1] Ordinal odds ratio

[2] For the ordinal regression analysis, the very and quite difficult and not sure categories were merged.

Table 6.6: Site staff views on sharing results in future trials

	Overall	Webpage			Posted Printed Summary (PPS)			Email List		
		Basic	Enhanced	Odds ratio (95% CI)	No PPS	PPS	Odds ratio (95% CI)	No Invitation	Invitation	Odds ratio (95% CI)
	n (%)	n (%)	n (%)	p-value	n (%)	n (%)	p-value	n (%)	n (%)	p-value
Should the way you shared results with participants be the standard approach for other trials?										
No	16 (24)	6 (17)	10 (30)	0.39	9 (27)	7 (20)	1.70	8 (23)	8 (24)	0.84
Yes	52 (76)	29 (83)	23 (70)	(0.07 – 2.42)	24 (73)	28 (80)	(0.32 – 9.04)	27 (77)	25 (76)	(0.16 – 4.45)
				0.318			0.532			0.838
Would you do anything different for future trials?										
No	52 (79)	28 (82)	24 (75)	1.65	26 (81)	26 (76)	1.43	28 (80)	24 (77)	1.06
Yes	14 (21)	6 (18)	8 (25)	0.48 – 5.67)	6 (19)	8 (24)	(0.41 – 5.02)	7 (20)	7 (23)	(0.31 – 3.62)
				0.424			0.573			0.930

complex", "achievable", "not time-consuming", "working well", and having appreciated the "clear instructions" provided.

> *"It was very, very simple, and you basically gave me all the instructions I needed" GMTCI02: Trial Coordinator, medium site*

6.6 Resource implications of the Show RESPECT interventions

6.6.1 Who was involved in delivering the interventions?

The staff involved in sending out printed information (the Patient Update Information Sheet and Posted Printed Summary, if appropriate) were mostly nurses (55%), clinical trial coordinators (18%), trials administrators (16%) or data managers (7%) (Table 6.7). While there were statistically significant differences between those at sites randomised to No Printed Summary versus Posted Printed Summary, these differences are largely in the distribution between the different administrative roles (trial coordinators, administrators and data managers). There were no significant differences in the other randomisations.

The breakdown of staff involved in dealing with participants' queries is different, with more focus on the clinical roles, particularly nurses (74%) followed by oncologists (13%) (Table 6.7). There were no significant differences between the randomisations.

6.6.2 Time and cost to sites of delivering the interventions

The resources required from sites to share the results with participants include staff time for posting information and dealing with participant queries, and the costs of postage and stationery for sending out the information. Table 6.8 shows the estimated total costs per participant, and a breakdown by the different types of resources required. The average total costs to site were £23.11 per participant. While per participant costs were higher in the Printed Summary arm (£29.79) compared to the No Printed Summary arm (£15.37) (which is to be expected), this difference was not statistically significant (p=0.108). The differences between the other randomisations were not statistically significant. The biggest component of the total costs of sending out results was staff time to send out the printed information. On average it took 11 minutes of staff time per participant in the No Posted Printed Summary arm, compared to 46 minutes per participant in the Posted Printed Summary arm. This difference was statistically significant (p=0.002). This translated into a £16.72 higher cost of time spent posting information in the Posted Printed Summary group compared to No Posted Printed Summary, which was statistically significant (p=0.005). The amount of time spent dealing with queries

Table 6.7: Site staff involved in delivering the interventions

	Overall	Webpage			Posted Printed Summary (PPS)			Email List		
		Basic	Enhanced		No PPS	PPS		No Invitation	Invitation	
	n (%)	n (%)	n (%)	*p-value*	n (%)	n (%)	*p-value*	n (%)	n (%)	*p-value*
Staff involved in sending out printed information?[1]										
Research nurse, research practitioner, research radiologist or clinical nurse specialist	24 (55)	14 (61)	10 (48)		11 (55)	13 (54)		12 (52)	12 (57)	
Clinician	0 (0)	0 (0)	0 (0)		0 (0)	0 (0)		0 (0)	0 (0)	
Clinical trial coordinator or research manager	8 (18)	5 (22)	3 (14)	*0.662*	6 (30)	2 (8)	*0.050*	4 (17)	4 (19)	*0.720*
Data manager	3 (7)	1 (4)	2 (10)		0 (0)	3 (13)		1 (4)	2 (10)	
Trials administrator	7 (16)	2 (19)	5 (24)		1 (5)	6 (25)		4 (17)	3 (14)	
Other	2 (5)	1 (4)	1 (5)		2 (10)	0 (0)		2 (9)	0 (0)	
Staff involved in dealing with participants' queries?[2]										
Research nurse, research practitioner, research radiologist or clinical nurse specialist	23 (74)	15 (79)	8 (67)		12 (71)	11 (79)		10 (77)	13 (72)	
Clinician	4 (13)	3 (16)	1 (8)		2 (12)	2 (14)		2 (15)	2 (11)	
Clinical trial coordinator or research manager	1 (3)	0 (0)	1 (8)	*0.306*	1 (6)	0 (0)	*0.558*	0 (0)	1 (6)	*0.575*
Data manager	1 (3)	1 (5)	0 (0)		0 (0)	1 (7)		0 (0)	1 (6)	
Trials administrator	1 (3)	0 (0)	1 (8)		1 (6)	0 (0)		0 (0)	1 (6)	
Other	1 (3)	0 (0)	1 (8)		1 (6)	0 (0)		1 (8)	0 (0)	

[1] Proportion of those who said they had been involved in sending out printed information in each of the job roles

[2] Proportion of those who said they had been involved in dealing with patient queries in each of the job roles

Table 6.8: Resources used by sites to share results with participants, per participant

	Overall Mean (Std. dev.)	Webpage			Posted Printed Summary (PPS)			Email List		
		Basic	Enhanced	Mean difference (95% CI) *p-value*	No PPS	PPS	Mean difference (95% CI) *p-value*	No Invitation n (%)	Invitation n (%)	Mean difference (95% CI) *p-value*
Total costs (primary outcome for site staff data), GBP	23.11 (27.00)	22.20 (32.73)	23.97 (20.93)	1.91 (-14, 18.74) *0.819*	15.37 (17.13)	29.79 (32.18)	13.71 (-3.19, 30.60) *0.108*	24.43 (33.71)	21.72 (18.29)	-2.87 (-19.70, 13.95) *0.731*
Estimated number of hours taken to send out all printed information	0.49 (0.64)	0.36 (0.55)	0.61 (0.70)	0.26 (-0.11, 0.62) *0.161*	0.18 (0.16)	0.76 (0.77)	0.59 (0.22, 0.96) ***0.002***	0.53 (0.73)	0.45 (0.55)	-0.08 (-0.44, 0.28) *0.657*
Estimated cost of time spent posting all information, GBP	14.10 (19.08)	11.81 (19.35)	16.28 (19.03)	4.71 (-6.53, 15.96) *0.401*	5.13 (4.65)	21.85 (23.22)	16.72 (5.43, 28.01) ***0.005***	15.59 (22.60)	12.54 (14.96)	-3.25 (-14.50, 7.99) *0.561*
Approximate number of participants who had queries	0.34 (0.49)	0.44 (0.53)	0.25 (0.44)	-0.19 (-0.49, 0.11) *0.198*	0.45 (0.58)	0.25 (0.38)	-0.23 (-0.52, 0.07) *0.131*	0.33 (0.46)	0.35 (0.53)	0.03 (-0.27, 0.33) *0.840*
Estimated number of hours dealing with queries	0.17 (0.27)	0.19 (0.29)	0.15 (0.25)	-0.04 (-0.21, 0.13) *0.631*	0.21 (0.26)	0.14 (0.28)	-0.08 (-0.25, 0.09) *0.343*	0.12 (0.23)	0.22 (0.30)	0.10 (-0.07, 0.26) *0.237*
Estimated cost of time spent dealing with queries, GBP	8.00 (16.08)	9.38 (16.64)	6.69 (15.81)	-2.85 (-13.06, 7.45) *0.583*	9.56 (17.02)	6.65 (15.49)	-3.63 (-13.92, 6.67) *0.480*	7.80 (18.88)	8.20 (12.99)	0.45 (-9.80, 10.71) *0.929*

	Overall	Webpage			Posted Printed Summary (PPS)			Email List		
	Mean (Std. dev.)	Basic	Enhanced	Mean difference (95% CI) *p-value*	No PPS	PPS	Mean difference (95% CI) *p-value*	No Invitation n (%)	Invitation n (%)	Mean difference (95% CI) *p-value*
Other costs, GBP	1.01 (0.38)	1.01 (0.36)	1.00 (0.41)	0.00 (-0.15, 0.15) *0.984*	0.68 (0.27)	1.29 (0.19)	0.61 (0.46, 0.76) *<0.001*	1.04 (0.42)	0.98 (0.34)	-0.08 (-0.23, 0.07) *0.310*

from participants was about 10 minutes per participant. This translated into a cost of about £8.00 per participant for the time spent dealing with queries, with no significant difference by randomisation. However, there was a suggestion that these costs may be lower in the Printed Summary and Enhanced Webpage arms. Other costs made up a small amount of the overall costs, although there was a significant difference between the No Printed Summary arm (£0.68) and the Printed Summary arm (£1.29) ($p<0.001$).

Most (26/41) sites reported spending between 0-1 hours in total sending out the Patient Update Information Sheet. Ten sites reporting spending 2-4 hours and three sites spent 5-7 hours in total. Only two sites reported spending considerably longer (12-13 hours) sending out the Patient Update Information Sheets. The sites randomised to the Printed Summary also reported the total amount of time spent posting the Printed Summary information. This was largely dependent on the number of participants at the site. 12/22 reported spending around 0-1 hours; 7/22 spent around 2-4 hours; and 3/22 spent 5-7 hours sending out the printed summary. 14/41 sites reported spending no time dealing with queries, while 21/41 spent up to an hour; 1/41 spent around 2 hours and 4 sites spent 3-4 hours dealing with queries. No sites reported spending more than 4 hours dealing with queries from participants.

Staff views on the time required to send out the information are discussed in Sections 6.5.2 and 6.5.5. Other resource implications to sites did not seem to be a concern, aside from one research nurse commenting that postage costs may be an issue for her site.

> *AMRNI05: "If it's a public post then it can be a bit of an issue for us if postage isn't supplied because budgets are tight."*
>
> *IV: Is there reluctance in your hospital to cover that sort of cost?*
>
> *AMRNI05: "Yes. Budgets are very tight." AMRNI05: Research Nurse, medium site*

6.6.3 Time and cost to the clinical trials unit of the Show RESPECT interventions

Developing, reviewing and implementing the Show RESPECT interventions took time from staff including a data manager, trial manager, programmer, statistician, communications specialist and clinical professor, with different associated costs. Table 6.9 shows the amount of time and cost of that time for the Patient Update Information Sheet, Basic Webpage, Enhanced Webpage, Printed Summary and Email List. The Email List was the most labour intensive intervention for the CTU, taking around 41 hours of staff time, which cost approximately £1695. This was followed by the Patient Update Information Sheet, (36 hours, £1545) and Printed Summary (26.5 hours, £1182 total). The

time and costs for the Enhanced Webpage (20.5 hours, £872 total) and Email Lists are underestimates, as they both largely use the same text as the Printed Summary, but the time spent developing this text is only counted in the Printed Summary row, to avoid double counting. The cost of the Basic Webpage were the lowest, although it benefited from plain English text having already been developed for the printed summary, requiring only restructuring and pruning for the Basic Webpage (13.5 hours, £564 total).

Table 6.9: Approximate time (hours) taken by CTU staff on developing, reviewing and disseminating the Show RESPECT interventions, and approximate cost of that time

	Development time (hours)	Testing/ reviewing time (hours)	Distribution time (hours)	Total (hours)	Approximate cost of time (GBP)
Patient Update information Sheet[1]	17	9.5	9.5	36	1545
Basic webpage	4	9.5	n/a	13.5	564
Enhanced webpage	11	9.5	n/a	20.5	872
Printed Summary	11.5	13	2	26.5	1182
Email list	22	17	2	41	1695
Total	65.5	58.5	13.5	119.5	5858

[1] The Patient Update Information Sheet is how the links to the basic webpage, enhanced webpage, email list were shared, along with opt-out information for the printed summary (i.e. the other interventions were not stand-alone without the Patient Update Information Sheet).

In addition to the staff time involved in developing, testing and distributing the interventions, the CTU also incurred printing and postage costs for sending the Patient Update Information Sheet and Printed Summary to sites. The average cost to the CTU per participant for the Patient Update Information Sheet was £0.61, coming to a total of £290. The average cost to the CTU per participant for the Printed Summary was £0.69, coming to a total of £125.

6.7 Discussion

6.7.1 Summary of key findings

The site staff who took part in the Show RESPECT study were strongly supportive of sharing results with participants, citing benefits including it being a way of showing that participants' contribution to trials are respected and valued, repaying trust, giving something back, increasing awareness of the importance of research, and helping participants process their trial experience. Concerns about the emotional impact the results may have on participants, and the practicalities of how the results are shared may act as barriers to sharing results, but these may be at least partially addressed through clinical

trials units providing sites with clear information co-produced with patients and the public. Despite strong support for the principle of offering all trial participants results, in practice trial results are often not systemically shared with participants, with Show RESPECT being the first experience of this for some staff who had worked across many trials for years.

The process used in Show RESPECT to share results with participants was generally seen as appropriate and feasible by site staff. Preparing participants to receive results was an important step in this process. Some site staff viewed the Patient Update Information Sheet alone as sufficient for this, while others felt more comfortable talking to the patients first to let them know what to expect, and some felt it should be covered in the informed consent process when participants join the trial. Sending out the printed information was generally reported to be easy and not too time-consuming, although staff at sites with large numbers of participants found it more of a burden. Site staff generally received fewer queries from participants about the results than they expected.

Providing results to participants in the form of opt-out Posted Printed Summaries increased costs to sites, with the bulk of that being staff time. It cost sites an average of £29.79 per participant to share results using opt-out Posted Printed Summary, compared to the £15.37 per participant in the No Posted Printed Summary arm. Most sites spent less than an hour sending out the Patient Update Information Sheet to all their participants. This was the same for sending out the Posted Printed Summary to all participants at sites randomised to that intervention.

The bulk of costs to the CTU was staff time for developing, testing, reviewing and distributing the interventions, with the Email List accounting for a third of that time. While developing, testing reviewing and distributing the interventions took staff time, the cost of this was well under 1% of the total costs of the trial to the clinical trials unit.

6.7.2 Strengths of this study

The range of sites included in this study, from District General Hospitals to specialist cancer hospitals, reflects the types of sites usually included in cancer trials run by the MRCCTU at UCL in the UK. Sites had between 1-52 eligible ICON8 participants. This allows us to be confident the findings around feasibility could be transferable to other UK cancer trials where sites have similar numbers of participants.

My study is the first to provide detailed information about the costs of sharing results with participants through different approaches, from both a site and

clinical trials unit perspective. This information will be of value to guide researchers planning and budgeting for sharing results with participants (something which the literature repeatedly recommends is considered, but provides no guidance on what resources are required).

As discussed in Section 5.3.2, the mixed methods design of this study is a strength, allowing us to gain a better understanding of the experience and views of site staff involved in sharing results with participants.

I reached inductive thematic saturation and data saturation at the 11th site staff interview. I cannot rule out the possibility that had I interviewed more site staff, additional insights may have been generated, but given the diminishing number of new concepts emerging in the last few interviews, it is unlikely to have substantially changed my findings.

6.7.3 Limitations of this study

A limitation to the generalisability or transferability of my findings is the possibility that site staff at sites which agreed to take part in a study about sharing results with participants may be more supportive of approach than site staff at other hospitals. This needs to be borne in mind when interpreting my findings.

Another limitation to this study is that the resource use data is only an approximation. Staff chose a category (e.g. 0-1 hours, 2-4 hours etc) rather than specifying the exact amount of time each task took them. The cost of this time is estimated from the generic approximations of the costs for that job family (medical, nursing or administrative staff for site staff, and role grade for clinical trial unit staff) taken from the National Institute of Health Research Schedule of Events Cost Attribution Template, assuming an Association of Medical Research Charities funder, for site staff, and WorkTribe assuming UKRI as a funder for CTU staff. We are missing site staff data from two sites, and we are missing data from five sites on time spent sending out the information, and 6 sites on time spent dealing with queries. This means there is some uncertainty around these estimates.

6.7.4 Conclusion

This chapter shows that there is strong support among site staff for the principle of sharing results with participants, and the process used within the Show RESPECT study is both acceptable and feasible for sites. The information on the process and resource requirements for the approaches used in Show RESPECT can guide others seeking to plan for sharing results in similar ways.

7. Patients' thoughts and feelings on receiving trial results

7.1 Overview of the scope of this chapter

This chapter explores patients' thoughts and feelings on receiving trial results and their reactions to receiving the results. It starts by exploring patients' motivations for joining the trial in the first place, as this may influence their desire to receive results and their reaction to those results. It then goes on to explore their expectations around whether they would be offered the results, and whether they wanted to receive them. It then looks at whether patients understand the range of potential outcomes a trial may have, as this may affect their reaction to receiving the results. It goes on to explore patients' reactions to finding out the results, including their intellectual response and emotional response. It finally explores patient and site staff views around sharing trial results with others, including family members of trial participants (including participants who die during trials); other patients and general practitioners. This chapter concludes with a short discussion of these results, including key findings, strengths and limitations.

7.2 Patients' motivation for joining the trial

Participants cited two main reasons for joining the trial: 1) they could personally benefit from trial participation, and 2) others could benefit.

> *"I just felt that, you know, whatever my possible chances were, if something I could do that was going to be part of my treatment might have meant that a) I could benefit, and b) you know, medical science could benefit by whatever was observed as part of the trial, and I had nothing to lose. I felt I had everything to gain." CSI01: Patient, small site*

This section explores those two motivations in more detail.

7.2.1 Personal benefits

Some women assumed that, for an intervention to have reached the point of being included in a trial, there must already have been considerable testing, meaning trial interventions are more likely to work than not work. As ICON8 was using established drugs, in a different dosing schedule, it was perceived to be low risk. Participants felt that it made sense that having more frequent, smaller doses of chemotherapy (as tested in ICON8) would be easier than large doses every three weeks. The evidence on this approach from previous Japanese trials was encouraging.

Chapter 7 Summary Box

Why was this study done?

- Participants wish to receive the results of research they have participated in
- Trial site staff may be reluctant to share results with participants because of fear of upsetting them
- It is important to understand participants' thoughts and feelings on receiving trial results to make sure that sharing results does not cause more harm than good

What did I do?

- I analysed qualitative and quantitative data from patients and trial site staff to explore patients' thoughts and feelings on receiving trial results

What did I find out?

- Patients join trials for potential **personal benefits** and to **help other people**
- Nearly all patients **wanted to know the results** of the ICON8 trial, to help them **understand if their aims for taking part were achieved**
- A large majority of patients were **glad** to find out the results of the ICON8 trial, despite some also being some being **disappointed** that weekly chemotherapy did not improve outcomes
- **Offering trial results to the families of participants who die during a trial may have value for the bereaved**, but **needs to be done sensitively** to avoid causing unnecessary distress

What do these findings mean?

- Participants should be offered the results of trials even when those results may be disappointing
- Further research is needed to explore how to share results with bereaved families of trial participants

Another personal motivation for joining the trial was the increased monitoring that trial participants receive, compared to those in standard treatment. This was reassuring for some participants.

> *"It was just about getting through what I needed to get through, and something that might give me a better opportunity of getting through it successfully. And also something that was going to give me an opportunity to be monitored for longer than I might have done*

otherwise, because [Research Nurse] explained to me that under normal circumstances I would be monitored routinely by the hospital for five years. But because I take part in the trial, I'd be monitored for ten." CSI01: Patient, small site

7.2.2 Altruism

For some patients, helping others was a key reason for taking part in the trial. Taking part in the trial was seen as a way helping future patients, or of giving something back to the NHS, or the doctors and nurses who looked after them. Taking part in a trial was framed by some as a good thing to have come out of their cancer experience. Others talked about having benefited from research that had been done previously, and participation in research being a way of paying it forward for future generations. Site staff also perceived altruism to be a key reason for participants agreeing to take part in trials.

"I just felt that mine had gone so unknown if there was any way that my participation could help, I don't know, future diagnosis or help future patients going through a treatment. Then I wanted to do that just to, if you like, just to put back a little bit into the system, into the NHS and see what comes of it." BLI01: Patient, large site

7.3 Patients' expectations around receiving results

Patients had differing expectations around whether they would receive the results. Among those who had not been expecting to receive the results, some had assumed that, as they were still in follow-up, results would not be available yet. Others had assumed that they would have died before the results were available. Some had put it out of their mind, while others remembered being explicitly told by their doctors that they would not be told the results. One interviewee talked about previously having participated in paid drug trials, and having not received results from that, so not expecting results from ICON8.

"I assumed that I would never know the results, that it would be… Well first of all I thought well I'll probably be dead anyway, but no, I didn't think they would be available. I thought trials probably went on for much longer, and that they would wait until people died before they assessed it." GSI01: Patient, small site

There was a sense among some site staff that patients' expectations around receiving results had shifted in recent years, with patients now being more likely to expect to receive them. This change in expectations may be because there is more discussion of the issue at the time patients join the trial.

"It's something that I think is becoming more important. A lot of our patients are becoming more empowered. They're wanting to seek more information. Treatment of cancer is becoming more complex, often patients will survive for longer and live with their cancer as a chronic illness. Probably there are more trial participants who are keen and

interested in finding out the results of studies that they have taken part in, in the past. It is becoming a greater priority for us to engage with them in this setting." HLCLI02: Clinician, large site

7.4 Patients' desire to receive trial results

A summary of findings from the patient qualitative data around patients' desire to receive results was published as Supporting Information to the participants results paper in *PLoS Medicine*[110].

7.4.1 Wanting to know the results

In line with the quantitative findings that 93% of respondents wanted to know the trial results (see Section 5.2.5), most of the women interviewed had wanted to receive the results of the trial. Most of the site staff interviewed said they thought trial participants did, generally, want to know trial results. The reasons site staff thought this were either because they had experience of patients asking for the results, or because they themselves would want to know if they were taking part in a trial. For several patients, their interest went back to when they joined the trial. Site staff talked about some patients asking when results would be available early in the trial. For some patients, interest in the results of the trial had been a motivating factor in signing up to be part of it in the first place. Other women said that when they joined the trial, learning the results was not a major focus for them because of the challenges they were facing at the time around dealing with a cancer diagnosis and chemotherapy.

"The whole point of when I joined the trial was because I wanted to know what the outcomes would be and how that would affect us in the future." DMI01: Patient, medium site

Some women had been actively seeking the results through the course of the ICON8 trial:

"I asked, well not all the time, but I used to see various consultants and when I saw the one that was the main one, I always would ask her, how's the trial going and what are the results looking like? And when can we see them? And all that kind of thing." DLI01: Patient, large site

One research nurse believed that patients who want to know the results will ask for them, so not being explicitly asked for results is a sign that patients did not want to know. However, other site staff felt that most would be interested to know, but only a minority will actively ask for results.

"I think if they were offered the opportunity to have the results or not, I think the majority of participants would be interested in seeing that information and reading that. From general experience, it does only seem to be the minority of patients who will actively seek that information out." HLCLI02: Clinician, large site

This chimes with one participant's view, who had wanted to know the results but hadn't actively sought them out. This has implications for whether an opt in or opt out process is most appropriate (see Section 8.6).

One participant said that she had lost interest in the trial, because nobody was talking about it following her chemotherapy (patients in the ICON8 trial have been followed up for several years after completing chemotherapy). When she received the Patient Update Information Sheet, she was surprised to receive it several years after her chemotherapy, but decided that she did want to know the results so accessed the webpage.

Some patients were keen to find out the results because they wanted to know how they had been affected physically by trial participation. For others, receiving the results was about knowing that they had contributed to something that may have an impact, and gaining closure. These motivations for finding out the trial results mirror the motivations for taking part in the ICON8 trial (see Section 7.2).

7.4.2 Not wanting to know the results

7% of patient questionnaire respondents did not want to be informed of trial results, and while site staff thought that most participants want to know trial results, there was recognition that not everyone does. This creates a need to be careful about whom you share the results with.

> *"I think what we need is before we can send to them, either we write them a letter to find out if they want, because some people want to forget about certain things. But then if we can phone them and say, we have got this which we can share with you, if you are interested. And if they say yes... I don't believe in just sending information without first asking for their consent or asking them if they're interested in doing this, because some do want to know and some don't want to know." BMRNI04: Research nurse, medium site*

One interviewed patient said she did not want to receive the ICON8 results as, although she herself was well, she did not want to find out that others in the trial had done less well. If, however, she had been on a trial for a less serious condition, she would have been interested in learning the results.

> *"If everything is fine, and all the ladies on the trial are fine, I would want to read that. If I was going to read it, and I found out that a very high proportion were not well, I don't want to see that. I'm probably putting my head in the clouds, or burying my head in the sand probably. But I'm very well at present, and I'm sure I'll stay well, but I don't… and there are always the seeds of doubt, you… Nobody who has cancer really is ever convinced that they're cured. I don't ever use that word, but I don't want to know about people. And you tend to hear about people who are not well and who have died. You don't hear about the people who are well. And I don't want to read something either in a letter, or on a computer*

that says such and such a proportion of ladies had died, or had got secondaries, or whatever. If everybody was fit and well, yes I'd read that." GSI01: Patient, small site

Other reasons reported by patient questionnaire respondents included worry about what the results would show, feeling like the results are not relevant to them now as their health situation had changed, or will not make any difference to their situation, and wanting to believe that the treatment they had was the best. Some had found it difficult to access or understand the results, which made them decide that they did not want to know them. Some site staff said that some patients did not want to be reminded about their cancer.

"We've got some patients here who obviously they don't want to talk about diagnosis, they don't want to talk about prognosis. So, again, I think receiving information like that through the post is sort of a reminder of, you know, the situation that they're in. And some don't really want to be reminded of that." HLRNI03: Research nurse, large site

7.5 Patients' understanding of potential trial outcomes

Communicating results to patients that go against their expectations of what the trial would show may be more difficult. It is important that participants understand the potential outcomes and have a sense of the prognosis of people like those in the trial, so survival results are not shocking. Site staff generally believed that patients, at the time of consent, understand the potential outcomes of the trial and their prognosis. But this understanding may be being constantly refined over the course of the trial and patients' interaction with site staff.

"We're always refining their understanding of the disease and we're sometimes at the beginning we're not as detailed because they can't absorb all the information. So, when they're on treatment many of them think they'll have perhaps a better outcome because being positive on their treatment, than perhaps the results may indicate. So, we have to constantly refine that as we see them." EBLMCLI02: Clinician, large and medium sites

Not all the women I interviewed had been in equipoise at the point at which they agreed to join the trial. Some had had strong views about which arm they wanted to be randomised to (weekly chemotherapy) because they believed it was likely to be gentler than having larger doses every three weeks. Some patients had tried to persuade site staff to allocate them to weekly chemotherapy arm. One participant was surprised and upset to be allocated to the control arm, having not understood that she would be randomly allocated to an arm.

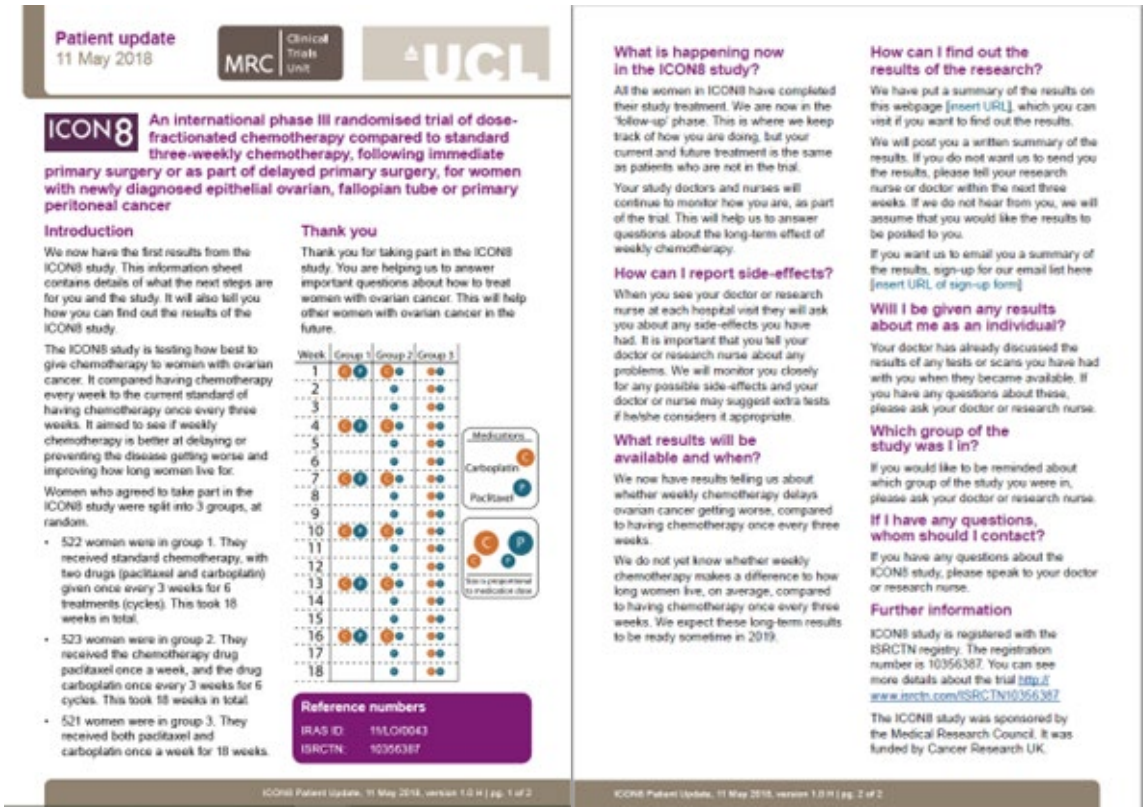
"I think I cried for about three days when I found out I was on the standard treatment really because it was a shock and the way that the information

was given to me in a telephone message. The computer has randomised you, standard treatment, bang." CLI01: Patient, large site

7.6 Patients' response to receiving the Patient Update Information Sheet

The first step in the communication of results for Show RESPECT (from the patient's perspective) was receiving the Patient Update Information Sheet (Figure 7.1), which thanked them for taking part, told them results were available, and how to access them (or, for those at sites randomised to the Posted Printed Summary, how to opt out of receiving it).

Figure 7.1: Patient Update Information Sheet (version for site randomised to webpage, Posted Printed Summary and Email list)



Patient update
11 May 2018

MRC Clinical Trials Unit

UCL

ICON8

An international phase III randomised trial of dose-fractionated chemotherapy compared to standard three-weekly chemotherapy, following immediate primary surgery or as part of delayed primary surgery, for women with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancer

Introduction

We now have the first results from the ICON8 study. This information sheet contains details of what the next steps are for you and the study. It will also tell you how you can find out the results of the ICON8 study.

The ICON8 study is testing how best to give chemotherapy to women with ovarian cancer. It compared having chemotherapy every week to the current standard of having chemotherapy once every three weeks. It aimed to see if weekly chemotherapy is better at delaying or preventing the disease getting worse and improving how long women live for.

Women who agreed to take part in the ICON8 study were split into 3 groups, at random.

- 522 women were in group 1. They received standard chemotherapy, with two drugs (paclitaxel and carboplatin) given once every 3 weeks for 6 treatments (cycles). This took 18 weeks in total.
- 523 women were in group 2. They received the chemotherapy drug paclitaxel once a week, and the drug carboplatin once every 3 weeks for 6 cycles. This took 18 weeks in total.
- 521 women were in group 3. They received both paclitaxel and carboplatin once a week for 18 weeks.

Thank you

Thank you for taking part in the ICON8 study. You are helping us to answer important questions about how to treat women with ovarian cancer. This will help other women with ovarian cancer in the future.

Week | Group 1 | Group 2 | Group 3

Medications: Carboplatin, Paclitaxel

Reference numbers
IRAS ID: 115LO/0043
ISRCTN: 10356387

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What is happening now in the ICON8 study?

All the women in ICON8 have completed their study treatment. We are now in the 'follow-up' phase. This is where we keep track of how you are doing, but your current and future treatment is the same as patients who are not in the trial.

Your study doctors and nurses will continue to monitor how you are, as part of the trial. This will help us to answer questions about the long-term effect of weekly chemotherapy.

How can I report side-effects?

When you see your doctor or research nurse at each hospital visit they will ask you about any side-effects you have had. It is important that you tell your doctor or research nurse about any problems. We will monitor you closely for any possible side-effects and your doctor or nurse may suggest extra tests if he/she considers it appropriate.

What results will be available and when?

We now have results telling us about whether weekly chemotherapy delays ovarian cancer getting worse, compared to having chemotherapy once every three weeks.

We do not yet know whether weekly chemotherapy makes a difference to how long women live, on average, compared to having chemotherapy once every three weeks. We expect these long-term results to be ready sometime in 2019.

How can I find out the results of the research?

We have put a summary of the results on this webpage [insert URL], which you can visit if you want to find out the results.

We will post you a written summary of the results. If you do not want us to send you the results, please tell your research nurse or doctor within the next three weeks. If we do not hear from you, we will assume that you would like the results to be posted to you.

If you want us to email you a summary of the results, sign-up for our email list here [insert URL of sign-up form]

Will I be given any results about me as an individual?

Your doctor has already discussed the results of any tests or scans you have had with you when they became available. If you have any questions about these, please ask your doctor or research nurse.

Which group of the study was I in?

If you would like to be reminded about which group of the study you were in, please ask your doctor or research nurse.

If I have any questions, whom should I contact?

If you have any questions about the ICON8 study, please speak to your doctor or research nurse.

Further information

ICON8 study is registered with the ISRCTN registry. The registration number is 10356387. You can see more details about the trial http://www.isrctn.com/ISRCTN10356387

The ICON8 study was sponsored by the Medical Research Council. It was funded by Cancer Research UK.

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7.6.1 Uncertainty about whether they received the Patient Update Information Sheet

Sites were meant to send the Patient Update Information Sheet to ICON8 participants, and logs from sites indicate they sent them to all eligible participants. However, some patients struggled to remember whether they had received the Patient Update Information Sheet, which may partly be a result of interview taking place several months after they had been sent the Patient Update Information Sheet, and also what else was going on in patients' life at the time the sheet was sent out (which, for some, included problems with

their own health, or having to care for sick relatives). It may also be that some Patient Update Information Sheets got lost in the post, and never made it to participants.

7.6.2 Actions on receiving the Patient Update Information Sheet

Patients described various actions they took upon receiving the Patient Update Information Sheet, starting with reading it or glancing through it and keeping the information. Patients at sites randomised to the Printed Summary did not need to take action to receive the results via Printed Summary, however some patients contacted their research nurse anyway, to say they wanted the results. For those at sites randomised to not have the Printed Summary, seeking out the results involved visiting a webpage, or contacting the site to ask for a printed copy of the results.

7.6.3 Thoughts on receiving the Patient Update Information Sheet

Patients generally welcomed the Patient Update Information Sheet.

> *"I thought, oh, it's interesting after all this time." CLI01: Patient, large site*

For sites randomised to the Printed Summary, the Patient Update Information Sheet explained that the Printed Summary would be sent in three weeks time, unless the patient opted out of receiving it. This was to enable patients who did not want the results the opportunity to opt out. But for some patients who did want the results, this seemed like an unnecessary step in the process. Others recognised that it may be necessary for other patients.

> *"For me it would have just been okay to receive the main report. And I wouldn't have needed any warning about it. But I understand that some people might think well why am I getting this, so I suppose it's a bit difficult." BLI01: Patient, large site*

7.6.4 Emotional responses to receiving the Patient Update Information Sheet

As the primary outcomes measured in ICON8 tend to take several years to occur, and recruitment to the ICON8 trial took place over several years, the Patient Update Information Sheet was sent out several years after patients had completed their treatment in ICON8, and patients' trial visits were now infrequent. For some patients, receiving the Patient Update Information Sheet was a surprise.

> *"It did come out of the blue, I suppose, because like I say, you tend to put it all out of your head, don't you?" FLI01: Patient, large site*

One patient spoke about feeling apprehensive about what the results would show. However, that apprehension was mixed with excitement. Others also reported feeling excitement about finding out the results. One patient, who had not wanted to learn the ICON8 results, said receiving the Patient Update

Information Sheet did not raise anxieties for her, and that she did not mind receiving the information sheet.

> *"I was in no way bothered by getting the letter, and I thought about it and decided that it wasn't for me, but I think the way it was handled, that was okay." GSI01: Patient, small site (did not want to receive the results)*

7.7 Patients' experiences of finding out the ICON8 results

7.7.1 Reading and processing the results

For some patients, reading and processing the results was something that took time, requiring several sittings to read small bits at a time, or re-reading the information, at their own pace, in order to get it clear in their head. Some patients particularly appreciated having a printed copy, which facilitated that gradual process. Some patients ascribed this need to come back to things several times to memory problems they had experienced as a side-effect of the chemotherapy. Others put this down to the emotional response to receiving the results.

> *"I think because when you first get some results like that, especially in my situation, you almost panic. You get the result but you panic. So, you read it and you're panicking, although you can see the outcome's good. So, you have to read it again to clear your mind, if you see what I mean." DMI01: Patient, medium site*

Some patients were only interested in learning the main result, and did not spend much time reading the results.

> *"Once I saw that basically they didn't seem to make a massive difference I don't think I looked to get any more details" FLI01: Patient, large site*

Those who had already received the results in another format (e.g. in person from a consultant, or via another Show RESPECT intervention) did not spend long reading the webpage information.

7.7.1.1 Reading the results with others

Just as, for some patients, their experience of cancer treatment and trial participation is something that they do together with loved ones, so too is finding out the results of the trial, reading the information together.

> *"Yes, my husband were there when the letter, he said, oh look, you've got a letter. When we looked in it, we were both reading it together." GSI02: Patient, small site*

7.7.2 How else did patients find out the results, besides their allocated approach?

Some participants reported finding out the ICON8 results in ways additional to their Show RESPECT randomisation, including being told the results by site staff, requesting printed copies of the results (for participants at sites not randomised to the Posted Printed Summary), searching for the results online, or finding them out through other ways.

7.7.2.1 Being told the results by site staff

The most common of these alternative ways of finding out the results was being told directly by their consultant, research nurse or trial administrator. 8 questionnaire respondents reported being told the results by site staff (research nurses or consultants, or both) in addition to the randomised Show RESPECT intervention(s). Sometimes this discussion was initiated by the patient. In other cases the impetus for discussing the results may have come from the member of site staff.

However, in some cases, patients asking for information on the results were rebuffed by site staff. One questionnaire respondent said in answer to the question on why she was very unsatisfied with how the results were shared said:

> *"Never advised on how I could obtain the results or had any discussions about the results. When asked about other patients told it was none of my business." AMQ05: Patient, medium site, randomised to Basic Webpage alone*

For two patients, the only way in which they found out the results was through being told by site staff. One patient, who is herself a medical doctor, gave this account of being told the headline results of the trial by her oncologist while she was undergoing chemotherapy for disease progression.

> *IV: "Can you tell me about how you found out the results of ICON8?"*
>
> *CLI02: "Oncologist."*
>
> *IV Okay, and did you initiate that conversation or did the oncologist?*
>
> *CLI02: "No. We talked. I was obviously sitting there a bit more frequently again because I was going through chemo, and we were chatting about what comes next, and then he went oh, by the way, it didn't work, ICON8."*
>
> *IV: "Okay."*
>
> *CLI02: "And that's probably because I'm a colleague, and a lot of the communication we have, not everything, I think it's quite interesting, I think the dynamics are… It was very much, it didn't work, or it might have been, not oh by the way, or you may have heard it's not worked, and so I went,*

all right, let's move on. I mean it's certainly not worked for me because I'm sitting here. And I didn't even say that, it was like, okay."

IV: "So you didn't ask any questions?"

CLI02: "No."

IV: "And it didn't make you want to go out and find out more?"

CLI02: "No because I trusted him to say if there had been a disadvantage of being in the arm that I was in, I trusted him to tell me that. So, having not gone and looked it up, I don't know that there really wasn't a disadvantage. I don't think there was. Because I would have thought he would have told me." CLI02: Patient, large site

7.8 Outcomes of finding out the ICON8 results

Finding out the ICON8 results led to several possible outcomes, including discussing the results with family, friends or health workers, reflecting on how the overall trial results compared to their own experiences, keeping the results for future reference, and sharing the results with others, such as other patients. The results also raised questions for some patients; this is discussed more in Section 7.9.1.4

7.8.1 Discussing the results with others

Once patients had received the results, some then discussed those results with others, including family members and friends, although these discussions may not have been in depth. Some patients had not discussed the results with friends or family, as they thought others would not understand, or be interested.

IV: "Have you discussed the results with anyone?"

GMI02: "I have done with my husband. Only my husband actually, really, because it's just me and him at home, my son lives away, so… And you know what youngsters are like there, as long as mum's okay now he's not really worried too much, really. But yes, I have with my husband, because he's obviously keen to know, so yes. And I probably have mentioned it a little bit to my mum as well, actually, come to think about it, yes."

IV: "And what sort of things did you talk about with your husband or your mum?"

GMI02: "Well, just really the overall results of the three different groups and how… I sort of told them how the group I was in, the second group, people had sort of more side-effects from that, so yes, that was the main thing." GMI02: Patient, medium site

Some patients had discussed the results with site staff.

"When I last saw [Research Nurse] at the hospital she was very busy, and we had a time for a little chat. And what amazes me is she remembers personal details about everybody. So, you know, it just makes you feel so special and so cared for. She obviously is very well informed on the results

of the trial, and she knows that I feel that I've been very lucky with it all. And she's just always so upbeat, always. It's amazing." CSI01: Patient, small site

However, several patients I spoke to had not yet discussed it with their clinical team, despite wanting to, as they were waiting for their next scheduled visit for an opportunity to do so. One patient said she would be more likely to discuss the results with her trial nurse, rather than other clinical staff, as she felt that the trial nurse would know more about the results.

7.8.2 Keeping the results

Many of the patients I interviewed showed me folders containing all the information they had received about the trial and their cancer treatment. In this context, patients appreciated having the printed summary that could be easily added to their files. Some women said if they had not received the Printed Summary, they would have printed out the information from the webpage, to allow them to file it for future reference.

"It was easy to read over a period of time and I could keep a copy without finding a printer." BMQ05: Patient, medium site

7.8.3 Sharing the results and their trial experience with others

Some of the women I spoke to were keen to share their experience of cancer treatment and being on a trial with other cancer patients. Some had been asked by site staff whether they would be willing to talk to others about taking part in trials.

"I would be very happy to communicate to people, and I did say that at the time to the team. If they have anybody who wants to talk about what it's like to be on a study, then they can come and talk to me because I can represent the patient participant, but also I know what it's like to be behind the scenes in an intervention trial, but also other types of studies. And I just uniformly think it's a very positive thing." CLI02: Patient, large site

One woman spoke about sharing the ICON8 results with other patients via the Ovacome online forum.

"When I was on there and I got the results, I actually went on and said, in case you're interested in the results, but it was basic just to say that it was the same. I didn't go into great depth, so I told them myself." BMI01: Patient, medium site

7.9 How did participants react to finding out the results of ICON8?

7.9.1 Intellectual response

A summary of the qualitative findings around participants' attitudes to the results was included as Supporting Information in the *PLoS Medicine* participants results paper[110].

7.9.1.1 Patients viewed the trial results as interesting

Most patients who were interviewed said that they had found the results interesting. This was also reflected in some of the comments in the questionnaires. For some, this interest was an abstract, intellectual interest. For others, the interest was more personal, stemming from finding out how women in their treatment group had done compared to the other groups and compared to their own experience.

> *"I thought there might be more of a difference but it seemed that really there was no change, except I think it was my group two, which I was on, which had more blood transfusions and things, so that was interesting. Because I had to have that myself, so you know then, that was normal." BMI01: Patient, medium site*

7.9.1.2 Patients viewed the trial results as important

Most patients who were interviewed said they thought the trial results were important. For some that importance was about the knowledge gained through the trial about the efficacy and side-effects of different treatment schedules, despite the interventions tested in ICON8 not proving to provide a benefit.

> *"I think it is an important result because I think that we need to know whether we're targeting in the right way." DMI01: Patient, medium site*

The importance of the results may be more personal for some participants, as receiving the results gave them closure.

7.9.1.3 Patients' interpretation of the results and their implications

Most patients who were interviewed seemed to understand the results and their implications (see Section 5.2.7). Despite the trial not finding any benefits from the interventions tested, patients still felt the trial had been worthwhile, either through ruling out a potential treatment, or providing data that might eventually lead to something in the future that may help other patients. This was cited as a reason for being pleased to have received the results.

> *IV: "Do you think these results will help in some way?"*
>
> *FLI01: "Well, yes, because it rules out, potentially rules out a method of treatment." FLI01: Patient, large site*

The resource implications of the results for the NHS was something that participants were interested in, speculating that three-weekly treatment was likely to be cheaper to the health system than weekly treatment, which was seen as a good thing.

> *"I guess if you're just treating people every three weeks, it's cheaper, so therefore in some countries that might be crucial in how many people you treat, so that might be of significance. So, that's quite an important thing." FLI01: Patient, large site*

However, some were concerned that cost considerations may be driving the researchers' interpretation of the trial results. Other patients discussed the cost and time implications of weekly versus three-weekly chemotherapy cycles for patients, with three-weekly cycles reducing transport and parking costs.

7.9.1.4 The results raised questions for some patients

Site staff expected to receive questions from patients who had received the results. The results of the trial did raise questions for some patients, although perhaps not as many as trial staff anticipated. For some patients, questions were around clarifications about the contents of the results summaries, or how their individual circumstances compared with the overall averages. For some these questions focused on the results for specific subgroups (which were not presented in the results summaries), such as by country or by disease stage when they joined the trial. Section 6.5.3 discusses how confident site staff felt about dealing with queries from patients.

Many of the questions raised by interviewees were around side-effects, including side-effects that were not mentioned in the results summaries, such as hearing loss, osteoporosis, allergic reactions, what factors influenced whether or not people got side-effects, and what 'severe side-effects' means. Some patients wondered what their side-effects would have been like if they had been randomised to a different arm.

> *"I did go through the mill a bit back in those days and yes, I can… I mean, severe side-effects obviously on the purple group was at just over 60%, so… And then the bloods… I mean, I had to have blood transfusions before chemo sometimes and sometimes leave a week because I wasn't well enough. And anaemia as well and things like that, so I did have that, and then the numbness and pins and needles and all that. Yes, I had it all. Yes. So, I did… Which I suppose, if anything, because I was keen to look at the group I was in and sort of read those results, then part of you thinks well, would I have felt a little bit better had I been in a different group? You know, but that's the whole point of being in it, isn't it?" GMI02: Patient, medium site*

One woman (who received results via the Basic Webpage, which did not cover this) had questions about the implications of the results for the treatment of future future patients.

> *"Does that mean that the regime is changing, has changed, or won't change? Are people still offered a difference in the way these treatments are given, or is it just going to be a standardised thing in future?" CSI01: Patient, small site*

Receiving the results also triggered some questions about the trial itself, such as how much longer they would remain in follow-up, or why the trial took place where it did.

Site staff also talked about some patients having questions, with one clinician talking about receiving the results empowering patients to ask questions. However, site staff had not been overwhelmed by questions, or patients requesting additional appointments to discuss the results, even at large sites.

> *"It's been dealing with, as you say, some questions that patients have raised. I have had one or two patients who I've seen for their routine trial follow-up, who have been part of that, who've felt empowered maybe from sharing those results… To delve into things a little bit more in detail." HLCLI02: Clinician, large site*

The information provided was sufficient for some patients, not raising questions.

> *IV: Did you have any questions about the results?*
>
> *GMI02: "Well, no, because they sort of spoke for themselves, really. I think because the results were made quite clear and the outcome, like I said, that they're going to just stick to the every three weeks and that sort of told everything I needed to know." GMI02: Patient, medium site*

One research nurse at a large site said she thought that a lot of her patients had not looked at the information that had been sent to them. Not receiving questions or feedback from patients was interpreted by some as meaning that patients were not interested in the results. Another hypothesised that patients may have had questions, but forgotten them by the time they had their next clinic visit.

> *"I've not really received any phone calls from any of the patients, you know, asking further questions about the results which, again, makes me think did they read the information in the first place?" HLRNI03: Research nurse, large site*

7.9.2 Emotional responses to receiving trial results

Quantitative and qualitative results around participants emotional responses to receiving trial results were included in the *PLoS Medicine* participant results paper and associated Supporting Information[110].

7.9.2.1 Surprise at the results

Several patients mentioned being surprised at what the results showed. This surprise came from their expectations that weekly treatment would be better or at least gentler than three-weekly treatment. Conversely, one patient, who had had weekly treatment and experienced side-effects, was expecting that the trial would find the three-weekly treatment schedule was better based on her experience, so was not surprised by the results.

> *GSI02: "When I were having this treatment done, I thought as I were having the treatment done, that the one that came out on top was the one every three weeks. I thought that would be the better one anyway."*
>
> *IV: "So you guessed right?"*
>
> *GSI02: "Yes, because I knew by what I had had, the weekly one. How it affected me, although it tended to… Affected everybody, but how it affected my blood. I thought probably that would work out better for it were giving your body a better chance of what would you say… It were giving your body a better rest, I should say, in between the doses. So, it didn't come as a shock, if that's what you mean." GSI02: Patient, small site, weekly chemotherapy*

7.9.2.2 Positive emotional responses

Nearly all (127/145 (88%)) of the patients who returned the questionnaire reported being glad they had found out results (Table 7.1). There was no evidence of differences between the Show RESPECT randomisations on this outcome. For some women, particularly those on the control (three-weekly chemotherapy arm), receiving the results gave them reassurance or relief, as it told them they had not missed out on a superior treatment.

> *"I think for me it's quite reassuring because it wouldn't have made any difference to me whether I'd had it weekly or every two weeks or the same drug every week for the smaller doses, you know, a month here or there." BLI01: Patient, large site, control group*

Some site staff said they had received positive feedback from participants, who had found the results reassuring or encouraging. That does open the question of whether emotional responses to receiving the results would have been different had the results shown a clear benefit from one of the arms (see Section 9.2.3).

> *"A lot of them were relieved because most of them were put onto the three-weekly arm when they wanted to be put on the weekly arm. So they were relieved to find out that it wouldn't have made a difference to their progression or relapse rate, as some of them had unfortunately relapsed. But they were, I think, happy to find that their treatment arm was just as good as the other treatment arm." CLTCI04: Trial coordinator, large site*

Receiving the results of the trial was a positive experience for some women because it made them feel part of something big and worthwhile, and gave them a sense of completion.

> *IV: "Are you glad you found out the overall study results?"*
>
> *DLI01: "Oh yes, definitely."*
>
> *IV: "Why do you think that is?"*
>
> *DLI01 "Because it was worthwhile, it makes it more worthwhile having done it. I think it doesn't leave anything unfinished or in the air or doesn't leave me wondering so that I know that it's been completed and all these other women have taken part. It's quite special really, I suppose, 1,500 women in the world from different countries and we've all been part of the same thing. It's quite powerful stuff." DLI01: Patient, large site*

7.9.2.3 Negative or mixed emotional responses

Only 4/138 (3%) reported regretting finding the results. 23/140 (16%) of participants strongly or slightly agreed that they found the results upsetting (Table 7.1). This is very similar to the proportion of site staff who reported patients being upset by the results (17%) (Table 7.2). There was no evidence of significant differences between the Show RESPECT randomisations on these outcomes. The proportion of patients finding the results upsetting is higher than the proportion regretting finding out the results, suggesting that while some participants were upset by the results, they did not regret having received them. For most patients receiving the results was, overall, a positive experience, but one that was tinged for some with more negative emotions as well.

The results of ICON8 were disappointing to some, as they did not show a benefit from one of the new treatment schedules. That disappointment was tempered by the understanding that you need to do trials to find out whether treatments work. This disappointment was also felt by some site staff, who talked about the need to share that sense of disappointment with participants. None of the patients I interviewed regretted taking part in the trial, or receiving the results.

Table 7.1: Patients' emotional response to receiving the ICON8 results

	Webpage			Posted Printed Summary (PPS)			Email List			
	Basic n (%)	Enhanced n (%)	Unadjusted OR (uOR)[1] (95% CI) p-value Adjusted OR (aOR)[2] (95% CI) p-value	No PPS n (%)	PPS n (%)	Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value	No Invitation n (%)	Invitation n (%)	Unadjusted OR[1] (95% CI) p-value Adjusted OR[2] (95% CI) p-value	Overall n (%)
I am glad I found out the trial results[3]										
Strongly disagree	0 (0)	2 (3)	uOR: 0.79 (0.38 to 1.65) p=0.533 aOR: 0.84 (0.40 to 1.75) p=0.638	0 (0)	2 (3)	uOR: 1.69 (0.81 to 3.50) p=0.161 aOR: 1.69 (0.81 to 3.53) p=0.162	1 (2)	1 (1)	uOR: 0.80 (0.39 to 1.67) p=0.555 aOR: 0.76 (0.36 to 1.62) p=0.475	2 (1)
Slightly disagree	1 (1)	1 (1)		0 (0)	2 (3)		0 (0)	2 (3)		2 (1)
Neither	7 (10)	7 (9)		9 (14)	5 (6)		5 (8)	9 (11)		14 (10)
Slightly agree	12 (17)	13 (17)		14 (21)	11 (14)		13 (20)	12 (15)		25 (17)
Strongly agree	50 (71)	52 (69)		43 (65)	59 (75)		47 (71)	55 (70)		102 (70)
I regret finding out the trial results[4]										
Strongly disagree	53 (79)	48 (68)	uOR: 1.51 (0.74 to 3.01) p=0.253 aOR: 1.41 (0.68 to 2.92) p=0.354	45 (70)	56 (76)	uOR: 0.93 (0.46 to 1.88) p=0.850 aOR: 0.94 (0.46 to 1.91) p=0.856	48 (76)	53 (71)	uOR: 1.51 (0.74 to 3.08) p=0.253 aOR: 1.51 (0.72 to 3.16) p=0.279	101 (73)
Slightly disagree	3 (4)	9 (13)		7 (11)	5 (7)		7 (11)	5 (7)		12 (9)
Neither	9 (13)	12 (17)		10 (16)	11 (15)		8 (13)	13 (17)		21 (15)
Slightly agree	2 (3)	1 (1)		2 (3)	1 (1)		0 (0)	3 (4)		3 (2)
Strongly agree	0 (0)	1 (1)		0 (0)	1 (1)		0 (0)	1 (1)		1 (1)
I found the results upsetting										
Strongly disagree	40 (59)	35 (49)	uOR: 1.26 (0.66 to 2.41) p=0.485 aOR: 1.24 (0.65 to 2.39) p=0.514	35 (55)	40 (53)	uOR: 1.21 (0.64 to 2.30) p=0.564 aOR: 1.31 (0.68 to 2.51) p=0.421	39 (61)	36 (47)	uOR: 1.68 (0.87 to 3.23) p=0.123 aOR: 1.54 (0.79 to 3.00) p=0.206	75 (54)
Slightly disagree	5 (7)	7 (10)		6 (9)	6 (8)		4 (6)	8 (11)		12 (9)
Neither	11 (16)	19 (26)		15 (23)	15 (20)		14 (22)	16 (21)		30 (21)
Slightly agree	7 (10)	9 (13)		8 (13)	8 (11)		2 (3)	14 (18)		16 (11)
Strongly agree	5 (7)	2 (3)		0 (0)	7 (9)		5 (8)	2 (3)		7 (5)

[1] Adjusted for strata, randomisation phase (early vs late) and clustering

[2] Adjusted for age, education level and internet use as well as strata, randomisation phase (early vs late) and clustering

[3] For calculating the odds ratios, the strongly disagree, slightly disagree and neither agree nor disagree categories were merged for this variable

[4] For calculating the odds ratios, the neither agree nor disagree, slightly agree and strongly agree categories were merged for this variable

Table 7.2: Site staff reporting patients being upset by receiving the results

		Webpage			Posted Printed Summary (PPS)			Email List		
	Overall	**Basic**	**Enhanced**	**Odds ratio**	**No PPS**	**PPS**	**Odds ratio**	**No**		**Odds ratio**
	n (%)	n (%)	n (%)	**(95% CI)**	n (%)	n (%)	**(95% CI)**	**Invitation**	**Invitation**	**(95% CI)**
				p-value			**p-value**	n (%)	n (%)	**p-value**
Do you remember any participants being upset?										
No	29 (83)	15 (75)	14 (93)	0.17	17 (94)	12 (71)	4.41	13 (93)	16 (76)	4.74
Yes	6 (17)	5 (25)	1 (7)	(0.01 – 2.28)	1 (6)	5 (29)	(0.34 – 56.79)	1 (7)	5 (24)	(0.32 – 69.81)
				0.183			0.255			0.257

"I was a bit disappointed really, because I thought, well, gone to all this trouble, and that's obviously not a crucial factor. But on the other hand, when you think about it, at least they've eliminated that as a potential factor. So, that's the way it works, isn't it, that's what you have to do, you have a theory, and test it." FLI01: Patient, large site

None of the women I interviewed said that they had found the results upsetting, although from the quantitative results we can see that some women had been upset by the results. One respondent to the questionnaire said that she had found some of the terminology used to explain the outcome measure upsetting, rather than the results themselves. This echoes discussion in the Patient and Public Involvement discussion group around the wording of the explanation of progression free survival (Section 4.4). Other site staff said that some patients had fedback negatively around receiving the results, with some patients being concerned or disappointed by the average survival times presented in the results. One patient, who had not experienced severe side effects, said that reading about the side effects other patients had experienced during the trial made her feel sorry for them.

For some patients, their emotional reaction to the results changed over time, with the initial negative emotional reaction being tempered.

"The initial disappointment that I felt, it's obviously softened with time" CSI01: Patient, small site

7.9.2.4 Reflections on the results and their randomised treatment allocation

When reflecting on the results during the interviews, patients often related the overall trial results to their experiences during the trial, such as how they compare to the broader trial population, how their side-effects compared to others, and how quickly their disease has progressed. Some patients seemed to find some comfort in knowing they were not the only people to experience those side-effects.

"In a way it was nice to see, in a way, and about how it affected different people. I thought when I started, oh no, I couldn't have been only one with blood low, in that one I were in." GSI02: Patient, small site

Having learnt the results, and had time to reflect on them, patients were generally glad of which treatment arm they had been allocated to (regardless of which arm that was). Patients who had initially been disappointed to be in the control group of ICON8 talked about now being happy to have been in that group.

"I feel quite smug about that because I feel quite happy that I did it that way because from your results, there isn't a lot of difference between the way the treatment was given.... it's just that instead of feeling ill all the time, I did have a week where I felt better and then you get back to the next stage." DMI01: Patient, medium site, three-weekly chemotherapy

Patients who had been randomised to weekly chemotherapy gave various reasons for being glad of their randomisation. For one woman, who did not have people around her whom she could talk to about her cancer, seeing the treatment nurses every week during the chemotherapy was beneficial. Another patient talked about the comradery that developed between the patients who received their chemotherapy weekly at the same time. For another, having chemotherapy weekly made her feel like something was being done.

> *"I think that it is worth pointing out that seeing someone every week, I found helpful. Even if you didn't particularly talk about anything, it was just the fact that you were there, and you felt that they were looking after you and stuff, and that you weren't on your own." FLI01: Patient, large site, weekly chemotherapy*

> *"It was really special every week with the people who shared that bay with me because we really had a laugh. And we did, yes, we did. It was outrageous. And we had a gentleman who was having treatment for his gastric cancer I think it was, who wanted to be in the bay with us because we were good fun." CLI02: Patient, large site, weekly chemotherapy*

7.10 Patient and site staff views on sharing results with others

7.10.1 Sharing results with participants in future trials

7.10.1.1 Advice for site staff

I asked interviewees what advice they had for site staff sharing trial results with participants in the future. The advice from site staff for other site staff ranged from preparing participants to receive results, finding out how they want to receive the results, ensuring the participant is well enough to receive results, keeping track of who the results have been sent to, making sure site staff understand the results in order to respond to questions, and offering support to participants.

> *"Find out what your patient wants, really, is probably the best thing to do. They might not want it face-to-face. They might just say, I'm happy to take something away. Actually it's always better to ask your patients first." AMRNI05: Research Nurse, medium site*

Most participants I spoke to did not have advice for site staff on this. The only things mentioned were the need to offer results (rather than assuming everyone wants them), and for results to be shared honestly and personally.

> *"Offer them to them, but understand that for some people, they prefer not to receive them, but certainly offer them." GSI01: Patient who did not want to receive results, small site*

7.10.1.2 Advice for clinical trials units

Site staff advice for clinical trials units included giving sites flexibility on the timelines in which the results are shared (to enable the results to be given to participants when they next come to clinic, for example), giving options on how results are shared with participants, making sure the wording is not too stark, and allowing sites to personalise information to be sent out.

> *"Give patients a choice. Don't put too stark information in the information… allow it to be personalised, unless the study centre is sending them out. If the study centre is sending it out, I don't know if that's the best thing either, but, yes, if it's to come from a site there should be some personalisation to it. But, again, that's easy for me to say because we're a small team with a small numbers of patients." DMRNI02: Research nurse, medium site*

Participant advice for clinical trials unit included framing the results in a positive way, and keeping the information simple and brief.

> *"Communicate it in a positive way. We have an answer. We didn't find a great positive difference, even the word positive is quite loaded. We didn't find that one arm was better than the other, but we have an answer because it means that we don't need to bring women every week. We can stick with the three weekly and they're as safe as each other. Because when you average it out the side effect profiles were fine, so that's a really good thing to know. So, frame it in a way that doesn't make people feel like they've contributed to something that's been a total waste of time because it hasn't... And you always find out lots of other interesting stuff along the way... So, there'll be lots of other things that come out. And that can be said. The main thing is, we have an answer to the question that we asked, and that's a really good thing to have, so now from there we move on. And there are lots of other little bits that help us answer lots of other little questions and you've helped us with that." CLI02: Patient, large site*

7.10.2 Sharing results with families of participants

7.10.2.1 Reasons for sharing results with participants' families

Both site staff and patients recognised that family members of trial participants are often heavily involved in trials, supporting participants to make decisions and come to clinic appointments. In some cases, family members as well as patients build close relationships with site staff. Family members may be interested to know trial results. They might find some satisfaction in knowing what their loved one had contributed to. In this context, it may be appropriate for them to have the option of receiving the overall trial results.

> *"Relatives and friends are very much involved in the patients' journey. And personally I would like to know the results if my loved one was participating in a trial." FLTCI02: Trial coordinator, large site*

7.10.2.2 Who gets to decide whether patients' families should receive trial results?

There were differing views over who should decide whether family members should receive trial results. Some patients wanted to be the ones to decide whether information gets passed on to family members, as they wanted to be able to spare family members from receiving worrying information.

> *BLI01: "I think that information should come from me to my family or to my friends not..."*
>
> *IV Not directly from the research team?*
>
> *BLI01: "No, I don't think so. I think it's something that if I want to share I will. But that's just me. Yes, I wouldn't want to put my family through anything worrying."*
>
> *IV Okay so it's you want to be able to shield them from it if necessary?*
>
> *BLI01: "Yes. If it was something, for instance, that my group had done really badly compared to the other groups, I wouldn't want them to know that." BLI01: Patient, large site*

Some women recognised that their partners may want different levels of information to what they wanted, and that their partners should have the option to receive information (e.g. about results) even if they personally did not want that information. These patients advocated for their loved ones to be given the choice of whether to receive results (regardless of what the patient decided for themselves).

> *"I make sure that absolutely wherever possible, my husband comes as well because, for me, the whole information seeking, and information giving and receiving is not just about me, it's about the other person, who is kind of co-diagnosed in a way. He needs to know just as much as I do, if not more so. So, I would think actually seeking the views of carers and partners would be incredibly important because for them it's a different ball game." CLI02: Patient, large site*

7.10.2.3 Practicalities of sharing results with families

There was general agreement that the question on whether family members should be informed of the results, and if so, how, could be discussed at the start of the trial with the patient and their loved ones, during the consent process. Staff at smaller sites felt more comfortable contacting family members, as they build relationships up with them over the course of the trial.

> *"So I feel like that should be in the consent form, right from the start, you know, in the event. Because we do have some trials where, you know, it states, if, in the unfortunate event of, you know, being unable to give consent, or in the event of a death, I would like the results to be given to a next of kin. So I feel like that should be mandatory in a consent form." FLTCI01: Trial coordinator, large site*

7.10.2.4 Should we share results with families of participants who die during a trial?

The issue of whether results should be shared with the families of participants who die during a trial was highly contested. Some patients and site staff felt that even offering them the results would not achieve anything, and be likely to cause upset, particularly if they learnt their loved one was on the worse arm, so it should be avoided. Others felt that it might be comforting for families to know that something was achieved through the trial that their loved one contributed to. Most interviewees recognised that different people would feel differently about it, and recommended asking family members. There was recognition that it would need to be done sensitively, and that that may be harder in some results scenarios. Some site staff felt that it should not be offered to family members of participants who have died unless they specifically ask for it.

> *"We're all different aren't we? Some relatives will be very upset, but others will be very interested. I think my family would be interested, but I don't think you can make an overall judgment because people are so very, very different, aren't they?" GSI01: Patient, small site*

7.10.2.5 Experience of sharing results with families of participants who have died during a trial

One trial coordinator I interviewed had experience from a previous study, where all the participants had died, where the trial team had asked for results letters to be sent to participants' family and friends.

> *"It was worded for what input their loved one had had within the trial. And we did have one person ring back and say she was quite distressed about receiving the letter, because obviously, it brought back a lot of the emotions. But the rest of them are quite positive and they actually want to be kept in the loop." GSTCI03: Trial coordinator, small site*

7.10.2.6 Who gets to decide whether we should share results with bereaved family members?

There was general agreement that the results of trials should not be sent to bereaved relatives without asking them if they wanted them first. Of those who felt that results should be offered to bereaved families, some felt this should be discussed with patients and their families at the time of joining the trial, as part of the informed consent discussions. Others felt relatives should be asked while the patient is still alive, but in poor health, or when the results are available, either via phone call from the doctor or nurse, or through sending a form for them to opt in.

> *"Just perhaps have a second interview. The first interview talking about the trial and then perhaps another interview just with the nurses, just to say whatever the outcomes are, where would you like the information to*

go? Or what would you like us to do with it? I think that might be useful. Certainly my husband when he was alive, he found it really difficult to cope with my diagnosis and treatment. But I think if he knew that they were going to see a result or an outcome, he might have… Unfortunately, he isn't here to see the end of the trial, but he probably would have liked the information to read in his own time really." DMI01: Patient, medium site

7.10.2.7 Practicalities of sharing results with bereaved families

Offering results to bereaved families without causing unnecessary distress was viewed as challenging by many interviewees.

"I don't know how you'd do that without stepping on people… That could be quite tricky because family members might actually want this information, but it's quite a sensitive conversation to have, isn't it?" GMTCI02: Trial coordinator, medium site

7.10.3 Sharing results with other patients

Some participants were interested in how the ICON8 results would be made available to other women with ovarian cancer who had not taken part in the trial, as they felt it may be of interest to them, and show that work was going on to improve treatment. They made suggestions about how this could be done, via summaries and posters in clinic waiting rooms, and patient support groups. Some participants had even proactively shared the ICON8 results with others via online discussion forums.

7.10.4 Sharing results with GPs

Patients generally felt that trial results should be sent to the GPs of participants, for their records, but recognised that GPs were so busy they were unlikely to read a results summary.

"I'm sure some GPs would want to know. I think you may wish to shorten it to about this much. For the purposes of the interview that's a paragraph. No advantages, no disadvantages and basically, we're now seeing whether the weekly thing works in conjunction with another drug. Thanks for continuing to look after your patient so well. That's probably it. It's a headline thing. And how are you going to get that to the GP so that the GP looks at it? No idea. Would my GP be interested? Well, I have such limited dealings with my GP, when I need something, I email him, and that's because by and large I sort out things myself. But I'm unusual in that way. But they're so snowed under with all these other things that they have to… But you'd have to ask them. How do you want to find out about trial results?" CLI02: Patient, large site

7.11 Discussion

7.11.1 Summary of key findings

Patients join trials for two main reasons: 1) potential personal benefits from access to improved treatment and/or monitoring; and 2) altruism, to help improve things for future patients, or give something back to their doctors and the NHS. 93% of participants had wanted to know the ICON8 results, to see if their motivations for taking part had been satisfied. Those who did not want to know were trying to protect themselves from learning information that may upset them. Participants generally understood that trials may not always find a benefit, but sometimes that understanding may take a while to emerge, and not all patients were in equipoise when they joined the trial, with some strongly wanting to receive weekly chemotherapy.

Patients generally found the ICON8 results interesting and important, and felt the trial had been worthwhile even though it did not find a benefit from weekly chemotherapy compared to three-weekly chemotherapy. The results did raise some questions for patients, although not as many as site staff were anticipating, which was sometimes misinterpreted as a sign of lack of interest in the results. 88% of participants were glad to have found out the results, while only 3% regretted finding out. However, 16% said they found the results upsetting. Some participants had been disappointed the trial had not found a benefit from weekly chemotherapy. Patients were generally glad that they had been randomised to the treatment arm they had been on, despite any initial disappointment in their randomisation, or the lack of benefit shown.

Offering trial results to family members, particularly of participants who die during a trial, may have value, but would need to be done sensitively. Further research is needed to explore how it can be discussed with patients and family members during the consent process of a trial, without causing undue distress.

7.11.2 Strengths of this study

Triangulating the qualitative findings from both site staff and participants is a strength of this study, allowing richer understanding of the issues raised, and for comparisons to be made between site staff perceptions and participants' views. For example, some site staff interpreted a lack of questions about the results as showing patients were not interested, but the patient data shows that they were interested, but the results did not always raise questions, or they did not want to bother site staff.

Triangulating the qualitative and quantitative results allows the qualitative findings to be put in the context of a broader range of participants and site staff, and gives us insight into what lies behind the quantitative results.

7.11.3 Limitations of this study

It may be that participants who found the results upsetting were less likely to agree to be interviewed, in order to protect themselves from having to relive an upsetting experience, meaning their experiences and views may be missed from my sample for the semi-structured interviews. This could explain why, while 16% of questionnaire respondents reported finding the results upsetting, none of the qualitative interviewees described finding the results upsetting, talking instead about disappointment or panic, but finding consolation in the trial answering the question it set out to. Instead, I have to rely on the free-text data from the questionnaires, which is less rich than interview data would have been.

The main limitation in the results around sharing trial results with family members is that I spoke only to participants and site staff, not family members themselves. Before any general recommendations for practice in future trials can be given on this topic, further research with family members of trial participants, including participants who die during a trial, is needed.

The research took place within the context of a single clinical trial, with a particular patient population (people with ovarian cancer), and with trial results that showed no difference. This means care is needed when transferring the results to other trials with different patient populations or results scenarios. Further research in different trial contexts could help explore to what extent the results are transferable, and what are specific to the context in which the study took place.

7.11.4 Conclusion

Trial participants should be offered the results of trials they have taken part in. Receiving the results can be a positive experience for participants, even if results do not provide a breakthrough that will change how future patients are treated. Patients can understand the importance of ‘negative’ results.

The next chapter explores which aspects of the mode of communication influenced participants’ satisfaction with how the results were shared. Lessons from this may help guide future trials to ensure the positive response to receiving results seen in Show RESPECT can be replicated in future trials.

8. What aspects of the interventions influenced patient satisfaction?

8.1 Overview of the scope of this chapter

In Chapter 5 we saw that the Posted Printed Summary increased patient satisfaction with how the ICON8 results were shared, and the Enhanced Webpage increased the proportion of people reporting the results summaries told them everything they wanted to know. This chapter explores data from site staff and patients around what aspects of the Show RESPECT interventions influenced patients' satisfaction with how the results were shared, in an attempt to explain these results. It starts by looking at patient and site staff views on communication mediums in principle (including printed summaries, electronic means of communication, and face-to-face approaches). It then explores patient and site staff views on the information contained within the ICON8 results summaries, including the language used, and information items which were seen as particularly important, unnecessary or missing. It then focuses on patient and site staff views about the information products used within Show RESPECT: the Patient Update Information Sheet; Basic Webpage; Enhanced Webpage; Posted Printed Summary and Email List. It goes on to examine the issue of personalisation in the context of sharing trial results, and whether results should be shared on an opt-in or opt-out basis. The chapter concludes with a short discussion of the key findings, the strengths and limitations of this study.

A summary of participant qualitative feedback on the Show RESPECT interventions was published as a supplementary table to the *PLoS Medicine* paper[110].

8.2 Views of patients and site staff on the communication medium

This section explores views of the communication medium in principle. Site staff and patients' preferences for communication medium fell broadly into one of four categories:

1. Approaches based on a printed summary
2. Electronic means of communication
3. A personal approach to results communication
4. Giving patients a choice of communication medium

Chapter 8 Summary Box

Why was this study done?

- Quantitative results from Show RESPECT showed that Posted Printed Summaries increased satisfaction with how the results were shared, but it is important to understand why, when thinking about how to communicate results to participants in future trials
- Having a better understanding of patient and site staff views on the Show RESPECT interventions could help improve the communication of results to participants in future trials

What did I do?

- I analysed qualitative and quantitative data from patients and site staff to explore their views on how results of trials should be shared with participants in general, and the Show RESPECT interventions specifically

What did I find out?

- **Printed summaries sent by post** were seen as **accessible to all**, especially those with limited computer literacy or access to the internet, and make it **easy for patients to keep information** for future reference
- The information contained in the results summaries tested in Show RESPECT **covered the topics participants were generally interested in**, and was **written in an understandable way**
- The **extra features contained in the Enhanced Webpage** (the short video, links to further information and support, and option to send in questions to be answered on the webpage) **may be useful for some participants**
- Some **personalisation** of the Patient Update Information Sheet (and Posted Printed Summary), such as including a personal covering letter or compliments slip, **was felt to be important** by some participants and site staff
- **Opt-out approaches to sharing results may be better** at ensuring participants who want to find out the results receive them, but the option to opt out needs to be made clear before results are shared

What do these findings mean?

- **Offering participants both a Posted Printed Summary and an Enhanced Webpage** may be a good way of ensuring ease of access, and providing ways to find additional information and support

8.2.1 Views on approaches based on a printed summary

Approaches based on a printed summary were preferred by many patients and site staff. For some this was because of ease of access for patients (particularly for those who were less confident with computers), and less chance of overlooking the results. Printed summaries were generally viewed as accessible to everyone. One patient, who was only mildly interested in the results because her cancer had already progressed, so she did not see the results as being relevant for her, had said that typing in a URL to find the results was a barrier to accessing them, but that she would be much more likely to read a printed summary sent to her by post, as it was less effort to access.

> *"Having a hard copy of the results made it easier for me to access and review the information thoroughly." HSQ02: Patient, small site*

Some favoured printed summaries as they preferred to reading on paper rather than on screens. Some site staff highlighted the advantages of giving information to participants to read at home, in their own time. Printed summaries facilitated this.

> *"It's easy and it doesn't put any pressure on the patients to give a response; if they want to there are details of how to get in touch but otherwise they can do what they want with the information." CLRNQ01: Research nurse, large site, preferred posted printed summary*

Some site staff and patients said they preferred printed summaries as it made it easier for participants to keep the information for future reference, and bring to clinic if they have questions. Many patient interviewees showed me the folders where they kept all the information they had received about the trial, including the Patient Update Information Sheet and Printed Summary (if randomised to that arm). Some, who had received the results via a webpage, talked about printing the information off to file it. Having paper copies also meant patients could annotate them. Another reason given for preferring a printed summary was it was seen as more discreet than other approaches.

Ease of sharing results for providers was given by site staff as a reason for preferring a particular approach. This was cited by some of those who preferred the posted Printed Summary.

Site staff often related their preferences to their perceptions of what patients would prefer. This was particularly the case for those providers who preferred the Printed Summary. Some linked this to how other information is communicated with patients, and patients being used to a particular approach.

Some patients were keen to share the results with family and friends. For some, having the results on paper made it easier to do this, whereas others thought having it as a hard copy limited their ability to share with others.

Sending information by post was seen by some staff as being more personal, giving the option to provide individual notes to patients. However, others would have preferred to have given the Printed Summaries in person, during a clinic visit, rather than post them out.

While many patients preferred receiving results via a Printed Summary sent by post, some patients and site staff were concerned about the cost and logistical implications of that approach. Chapter 6 discusses the resources required from sites.

> *"Maybe having your named contact, who in my case is [Research Nurse], maybe her having some of them to be able to distribute to people may be okay, but again it's down to resources. If you were to email it to her and say, print however many copies, is that an added expense that the hospital really would rather not have? So it's about who picks up the bill for all of this. You know, where the economies have to be made. It's life, isn't it, budgeting and making sure there's enough money to cover the costs of all these things?" CSI01: Patient, small site*

8.2.2 Electronic means of communication

Some patients preferred to receive results by email or webpage. For one patient, this preference was because of the speed of finding results, and not having to wait until the opt-out period has finished before getting the printed summary. Several patients were keen to be informed of the results via email. For some this was about saving resources for the NHS, compared to printed summaries, and for others it was seen as easier than having to access a webpage themselves. Others preferred to read the results on a webpage. Some thought the information would be easier to understand online, whereas for others it was easier to share a webpage with friends and family than a paper document.

In principle, most of the women I interviewed said they would be happy to receive results via email. One of the advantages of receiving results via email was that it was seen as more personal. Site staff identified other advantages of email as an approach to sharing results, including it being easier to file than a webpage, and to share with family and friends. A drawback of receiving results by email was the volume of emails people received, and the risk of emails getting lost within that.

For those site staff who preferred electronic means of communication, ease for patients was not one of the reasons for this preference, but ease for providers sharing the results was. However, at some hospitals site staff talked about challenges around hospital IT systems blocking certain email addresses, or email addresses being less easy to access, which made sending emails to

participants challenging. Others felt email addresses were more likely to remain current than postal addresses.

> *"Sending an email like this to the participants would be a really good idea for those who ask for the results. I think that would be really useful. Again we could just forward this email onto them quite easily. And so I think that would be a really quick, you know, and simple way of giving the results by doing that. So, I think that's a really good idea." HLRNI03: Research nurse, large site*

Many site staff and patients had concerns around using electronic means of communication, as they felt that many ICON8 participants do not have access to computers, email or internet. Where electronic means were preferred, this was often in combination with a printed summary for those who are unable to access the internet.

> *"I know quite a few that wouldn't bother and don't like things online anyway... I hate to say it but even my age group don't like getting things on email. They like it in their hand." BMI02: Patient, medium site, aged 71 or older*

The way the interventions were delivered in Show RESPECT, women who wanted to receive results by email had to visit a URL to sign up to the mailing list. For women who wanted the results immediately, it was quicker to access the website. And for those who were less concerned about speed, the Printed Summary was an easier option, as the opt-out approach meant they did not need to take action to receive it. Only one of the interviewees had tried to sign up to the Email List, but she had used an email account that had been closed due to inactivity, so she did not manage to subscribe.

8.2.3 Personal approaches

Several patients commented that they would have liked to have received results in a more personal way, through face-to-face or telephone conversation with their research nurse or consultant. For some it was about the opportunity for discussion and explanation, or the chance to hear what their research nurse or consultant thought about the results. Others said that they would feel more valued if they received the results in a more personal way. Another reason for preferring more personal communication of results is the relationship between patients and site staff, which is discussed in Section 9.3.3.1. Having that discussion would serve to draw attention to the results, which may be missed if sent by post or email.

> *"It'd be good to hear what they think, in a way, we were surprised, or, interesting? … The trouble is you get so much stuff, don't you, both through the post, and email, and this, that, and the other, that you have to find ways of drawing attention to it, don't you? So, the personal approach is good as well, if possible." FLI01: Patient, large site*

Some patients felt that finding out the results directly from site staff would be preferable to reading the information, as site staff would be able to make them more palatable. Some site staff felt uncomfortable not being able to gauge participants' reaction, and whether they needed further support.

> *"When you see it in black and white it's really final, isn't it. Whereas a health professional might be able to sugar the pill a bit." GSI01: Patient, small site, who had not wanted to find out the results*

Face-to-face conversations with site staff were seen as a good way of finding out the trial results. However, organising this needs to be approached with caution, as calling patients in for an extra appointment could cause anxiety. Where possible, combining the results discussion with a regular check-up was seen as a good approach.

Some patients and site staff advocated for mixed approaches, which combined one of the Show RESPECT interventions with more personal communication, to allow the opportunity for patients to ask questions, and for site staff to make sure patients properly understand the results.

> *"I think getting stuff through the post is fine, and maybe be followed up with a phone call, perhaps. Obviously it's people's time, isn't it, so you don't want to waste people's time that should be doing other things. But I think that might be a good idea, that'd be reasonably cost-effective I would have thought, so that if you've got any questions, you could ask them.*

> *"Plus also, some people might just get it completely wrapped round their ears and not understand it at all, and if they've been part of a trial you have got a certain responsibility to make sure that they do understand at least in general terms what it was about. As I say, I think the ideal thing is actually talk to somebody face-to-face. I would have thought the only way of doing that reasonably would be if you were there for another reason, and then you could just have five minutes and go through it, that would be good as well." FLI01: Patient, large site*

When talking about personal approaches to sharing results, several patients raised the resource implications, leading some to conclude that the drawbacks outweighed the benefits of more personal communication.

> *"I wouldn't have minded face-to-face, I suppose if you've got questions that's useful but it's a lot of waste of NHS money and time, when they can just send you something that you can read yourself." BMI01: Patient, medium site*

Another disadvantage of more personal approaches that patients raised was they felt that would take away the ability to process the results at their own pace, or be hard to take in.

> *"I think the way that it was offered, as documentary evidence that everybody could take in at their own pace, that's the best way to have done it." CSI01: Patient, small site*

8.2.4 Group meetings

Another approach to sharing trial results mentioned in interviews by some patients was group meetings, where trial participants are brought together, and the results shared with them. One of the advantages that patients identified with this approach was that it would give researchers a better idea on whether participants understand the results, and providing clarification where needed. However, other patients did not like this idea, as they preferred to have the opportunity to read and process the results privately. Other perceived drawbacks included the risk of it being depressing, and not reaching everyone who wanted to know the results. Site staff raised concerns about the feasibility of this approach.

> *IV: How about face-to-face meetings where you get together all the participants in one room and tell them the results?*
>
> *AMRNI05: "I've never done that, I would imagine it's very tricky to do, unless it was something which was done by the trial office but it would be impossible for a hospital site to arrange."*
>
> *IV Right. Is that just because of the costs involved or logistics?*
>
> *AMRNI05: "All of it. Costs, finding a room, yes, it just would be too difficult finding enough people to be there at the same time. It's very difficult." (Research nurse, medium site)*

8.2.5 Giving participants choice

Patients and site staff recognised that different patients have different preferences and needs when it comes to receiving trial results, and many recommended that researchers should give patients options on how to receive results, allowing patients to pick the option that best meets their needs. Some specified what these options should be (postal and website, or consultation and website). The combination of Printed Summary and Enhanced Webpage was popular as not only did it give patients the choice between physical and electronic information, but also the level of information, as the Enhanced Webpage contained more information.

8.3 What did patients and site staff think about the information contained in the results summaries?

8.3.1 The level and length of information contained in the summaries

Patients and site staff generally agreed that the information summaries used in Show RESPECT were pitched at the right level of knowledge, being neither too technical nor patronising.

"What I like, you don't treat them as if they're stupid, because they do know what stage they are. They're clued on to all of that, so that's good, you're not thinking they won't know." CSRNI01: Research nurse, small site

The Patient Update Information Sheet was sent to participants to inform them the results were available and how to access them. The Patient Update Information Sheet was tailored according to how each site was randomised. The Patient Update Information Sheet was two sides of A4. Information about how to access the results was on the second page of the sheet. However, not everyone had spotted that information. One clinician described the PUIS as quite "text-heavy", which may have contributed to participants missing that information. Others, however, had spotted that information, and appreciated being given links to information they could access if they wished.

"Apart from receiving the 'Patient Update' dated 11/5/2018 I have not been told anything else" CLQ02, Patient, large site, randomised to no printed summary

There were mixed feelings around the length of the Printed Summary, with some describing the Printed Summary as short, and a good length, whereas others thought it was too wordy and would benefit from being reduced in length.

"Well I personally think if it had been half as long, it would have been more interesting. I think all you've got to do is cut the words down." GMI01: Patient, medium site

The level and amount of content of the Enhanced Webpage was about right for some patients and site staff. Some site staff felt the chunks of information were too long or wordy, while others thought it was about right.

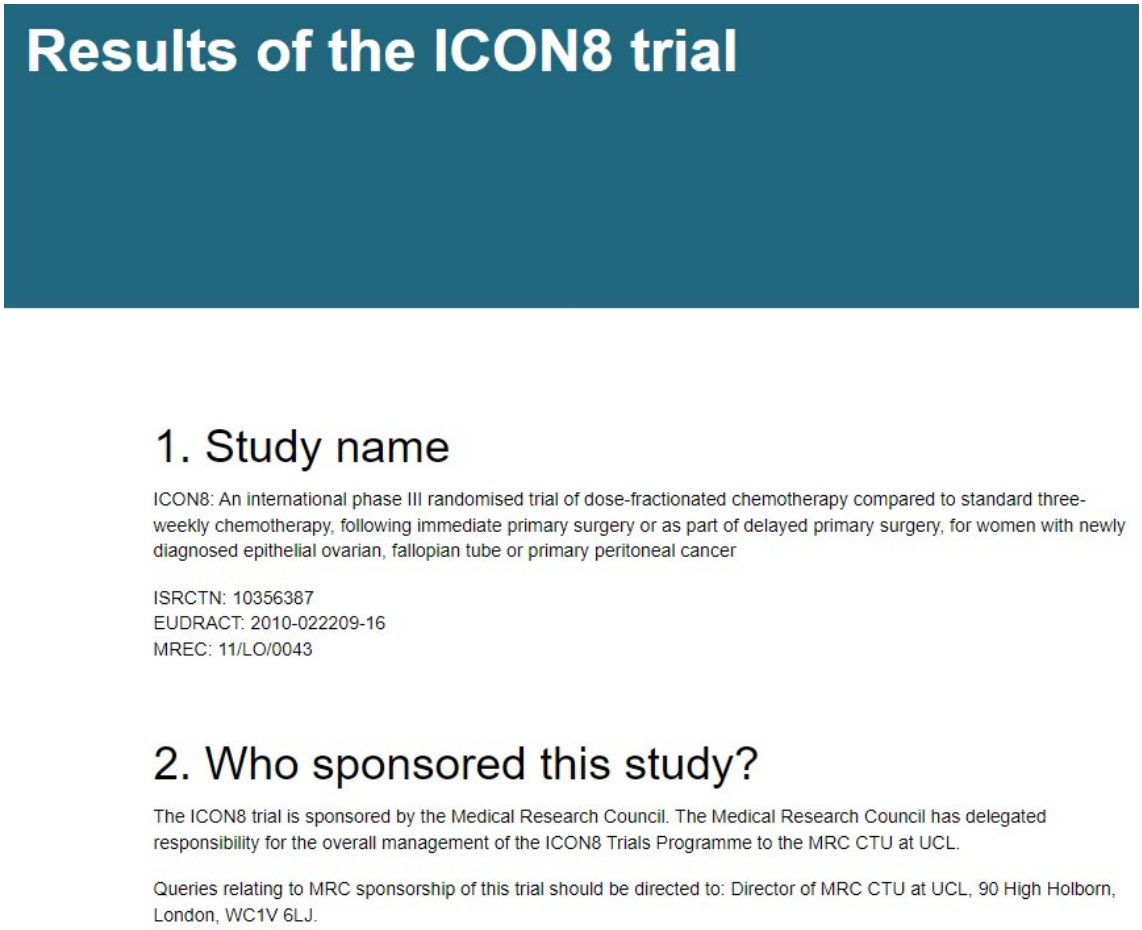
8.3.2 The language used in the summaries

Many people described the language as clear and easy to read, not using too much jargon. This was true for patients with different levels of education. However, a few people found the Basic Webpage information more challenging to understand. This may be because of the scientific terminology used in the early sections of the webpage, which includes the full scientific title of the ICON8 trial (see Figure 8.1), after which one patient said it got easier to understand. One suggestion to help with this was that a plain English glossary would be a useful addition to the Basic Webpage.

The tone of the writing was also noticed, with the Basic Webpage being described as being cold and less personal or conversational than the enhanced webpage. However, this did not hinder understanding.

"It doesn't seem as easy as to read as the enhanced one." HLRNI03: Research nurse, large site

Figure 8.1: Information at the top of the Basic Webpage



"I think that's better; even though it's a bit more cold, I think it's a bit clearer, to be honest." FLI01: Patient, large site

8.3.3 Interesting and important information

For some patients, the most interesting parts of the summary were those that related to the main efficacy results and their implications for patients. When talking about the results, patients often focused on the side-effects, relating what was presented in the summaries to their own experience. Site staff also felt that this would be interesting for participants. The reminder about the different groups in the trial was helpful to some patients, who may have forgotten which group they were in. Patients were also interested in the size of the trial, and where it was taking place.

"It was interesting to know how many people get a recurrence, because I've been lucky and I've not had a recurrence. But a lot of people do seem to." BMI01: Patient, medium site

The item identified as most important to patients by site staff was the section on 'What do these results mean?', which covered implications for the trial participant and for future patients. The implications for participants was not included in the Basic Webpage, and was identified by some site staff as something important that was missing from that webpage.

"What they really want to ask you is that is this treatment going to become the main treatment in future?" EBLMCLI02: Clinician, large and medium site

8.3.4 Unnecessary information

Some patients only wanted the headline result, finding the other information hard to understand or unnecessary.

BLI01: "Because even when the information came through you look at it and you think, really, pages I don't really understand all of that and I don't need to really. All I would have wanted to have seen was... And I think it was included in one of the results 50% of women who were on the three week, 50... Well, 20% on weekly or whatever just to have seen how those statistics had evolved."

IV: So, the headline results?

BLI01: "Yes, because the rest of it to me as a member of the public, I can't do anything with that information; it's not useful to me. But I would have been interested in as you say a headline result." (Patient, large site)

The Basic Webpage started with the full, scientific title of the trial, trial registration numbers and who the sponsor was (Figure 8.1). Some patients found this information hard to understand, and unnecessary, and some site staff thought patients would not be interested in this. However, one patient did pick this out as information that was important to her.

"I think the first, I'm not quite sure of the necessity to put all, I don't know what it means even, under number 1. Study name, it's quite professionally written from a lay point of view. And all those numbers and letters, goodness knows what that means. ISRCTN: 103… You know, for a lay point of view and even from my point of view, I suppose I'm somewhere in between being lay and not lay, it's gobbledygook really." DLI01: Patient, large site, retired nurse

8.3.5 Missing information

Some patients were frustrated that the Patient Update Information Sheet did not include information about the results.

"I think my husband's words were, well, it doesn't say anything, does it? And I remember, no actually, it doesn't really. It's all a bit too vague and glossing over the surface." DLI01: Patient, large site

Many patients felt that the results summaries they had received had told them everything they wanted to know (see Section 5.2.6 for the quantitative results relating to this). Site staff also felt that the Printed Summary, Enhanced Webpage and Email contained all the information patients were likely to want to know. Some felt that including any extra information would make it harder for patients to understand or put people off reading it.

"It's informative and you've got everything there that you could possibly need to know about the trial." BLI01: Patient, large site

Some patients and site staff would have liked there to be a brief summary of key points (the main result, and what it means for participants and future patients) at the start of the results summary.

Some patients talked about other information they would have liked to have seen, but there was no agreement over what should be added, with different participants interested in different things. This included:

- more information on side-effects
- information on overall survival (this information was not yet available at the time the progression free survival results were released)
- a reminder of which group they personally had been in
- information on how their individual results had compared to the overall results
- more detailed information about the demographics of the patients who took part in the trial
- more detailed breakdown of the results by subgroups
- more information on compliance with treatment
- more information about the study design
- putting the results into a wider context

8.3.6 Information on survival

Some site staff and patients were concerned about the information on survival times, with some participants saying they found it scary, and staff worried it would upset participants. However, the majority of site staff felt the wording of this information was good.

"The only thing that can give you a few wobbles sometimes is when it says that you roughly had around 24-25, that's 25 months, before cancer came back or got worse. It's almost like as if it's saying it will get worse or it will come back" GMI01: Patient, medium site

One clinician reported that it could be tricky for some participants to understand that they may have a different outcome from the average results.

"For patients they're not a statistic, they're an individual so they need to know that although we have population statistics and this is what some people do, it's not necessarily going to be their experience. And so, I've had a lady in [E Hospital] again who said she was on her five to six year follow up who had done pretty well. And she said to me 'but I was so disappointed with the results' and I turned around to her and said 'but that's not you, is it? You're an individual.' So, it can be very tricky

perhaps making clear to patients that this is a general picture but it's not necessarily going to be their particular journey that they'll be definitely in the middle of that result." EBLMCLI02: Clinician, large and medium sites

8.3.7 Diagrams

There were mixed opinions about the diagrams (which were in the Printed Summary, Enhanced Webpage and Email), with some patients and site staff finding them helpful and clear, as well as adding colour to the summary. One patient and some site staff thought the diagrams were unnecessary and/or unclear.

"That's the part that is very interesting but very clear because you can tell then from group one what the most common reported side effects are." BLI01: Patient, large site

"I think it's okay, but it just needs a little bit of looking at it more and I think for the women that I know are in follow up, they might not understand it so clearly." BMRNI04: Research nurse, medium site

8.3.8 Links to further information and support

The enhanced webpage and email contained links to further information and support. Some patients and site staff said that these links were helpful and good. Several patients talked about not needing the links to support services themselves, but that they might be useful for others who are less connected to support already. Site staff also felt the links to further support may be helpful for some patients, particularly if the results reawakened difficult emotions. One patient, who had found out the results from the Basic Webpage, felt that the basic webpage was missing information on how to access support. Against this needs to be weighed the drawback of adding to the length of the summary, which may make it harder for some patients to understand.

"I like that all of them let you know that if you do need further information, there are plenty of ways of obtaining it. And it's easy to actually get to the stuff. Sometimes it's a nightmare for when you go online and you're trying to find something, you can be half an hour searching your way around trying to get to it. But this is easy to get to everything. Support lines, you can't ask for more than that, can you really? Loads of different support lines and things you can have another look at." BMI01: Patient, medium site

"Particularly if sharing the results of the study reawakens emotions that were present initially, at initial diagnosis or initial treatment. Having some ability for that patient to get some additional emotional and psychosocial support is important. But also, if they have questions about the results and for whatever reason they are unable to get appropriate answers from their investigators, being able to go onto patient forums or nurse advisor lines, I think will be important for a proportion of trial participants." HLCLI02: Clinician, large site

8.3.9 Frequently asked questions

Both the Enhanced Webpage and Email offered the opportunity for patients to submit questions about the results, which would then be answered in the Frequently Asked Questions (FAQ) section of website or in the next email. Although only one patient submitted questions, many of those interviewed felt that it was a useful feature, which may be of value to others. One patient, who had difficulty understanding the results, did not want to send in her question because of worries about what others would think. Another patient disliked the anonymity of having questions answered through the webpage and would rather ask her research nurse. Site staff who were interviewed agreed that this feature was a good idea, in addition to being able to ask site staff questions. This was seen as being particularly useful for participants at large hospitals, who may not know the person they're speaking to at the hospital. Another perceived advantage of the FAQ section is that it may be quicker than trying to contact site staff.

> *"I think making results as accessible as possible and making sure that there is a facility for this to be a two-way process, within reason, is important. I would hope that most trial participants would be able to do that with their treating oncologist and research nurse, but if they're not, I think having the ability to do that with the trials unit, and the trial team, is important." HLCLI02: Clinician, large site*

8.3.10 Video of researcher summarising the main results

The Enhanced Webpage contained a short video of a trial doctor explaining the results. Many patients liked the video, finding it clear and even comforting or reassuring, and more personal than just reading the results. Several interviewees who had used the Enhanced Webpage had not looked at the video, having found the information they wanted from written information. Some felt that it would be useful for others, even if they themselves did not feel like they needed it. It could also be a useful way for patients to share the results with others, such as family members. The video was seen as being a good alternative to reading, particularly for people who do not enjoy reading. Some patients like the conversational tone of the video, while others had more mixed feelings about the delivery of the talk. One patient strongly disliked the video, feeling the tone and delivery was too sombre.

> *"So, in some way, having him talking about it is actually quite nice really. It's quite comforting I suppose because it's not just plain written word. It's actually somebody talking to you. I quite like that." DMI01: Patient, medium site*

Some patients picked up on the doctor's American accent, seeing this as negative. This relates to comments several patients made earlier in the

interviews about distrusting health information from American websites, as they view the US health system to be so different to the UK that information from the US was irrelevant or untrustworthy.

8.3.11 Thanks

The Basic Webpage did not contain a statement thanking participants, and one patient and several site staff picked up on this.

> *"I think the thank you at the start is something that's missing off of the other one [Basic Webpage]" DLI01: Patient, large site*

8.3.12 Other information

One thing several patients picked up on was that the date on the Patient Update Information Sheet was considerably earlier than they had received it. This delay is a result of the time needed to go through the various approvals and site set-up processes to run a study like Show RESPECT. Patients were unimpressed with how long it took to get them the information.

> *"From memory, I think it was vastly out of date so I would have received it in, I don't know, as an example, I received it in October and it was dated May or something. So it didn't impress me really." DLI01: Patient, large site*

8.4 Views on the Show RESPECT interventions

8.4.1 Layout and structure of the Show RESPECT interventions

8.4.1.1 General views about the layout

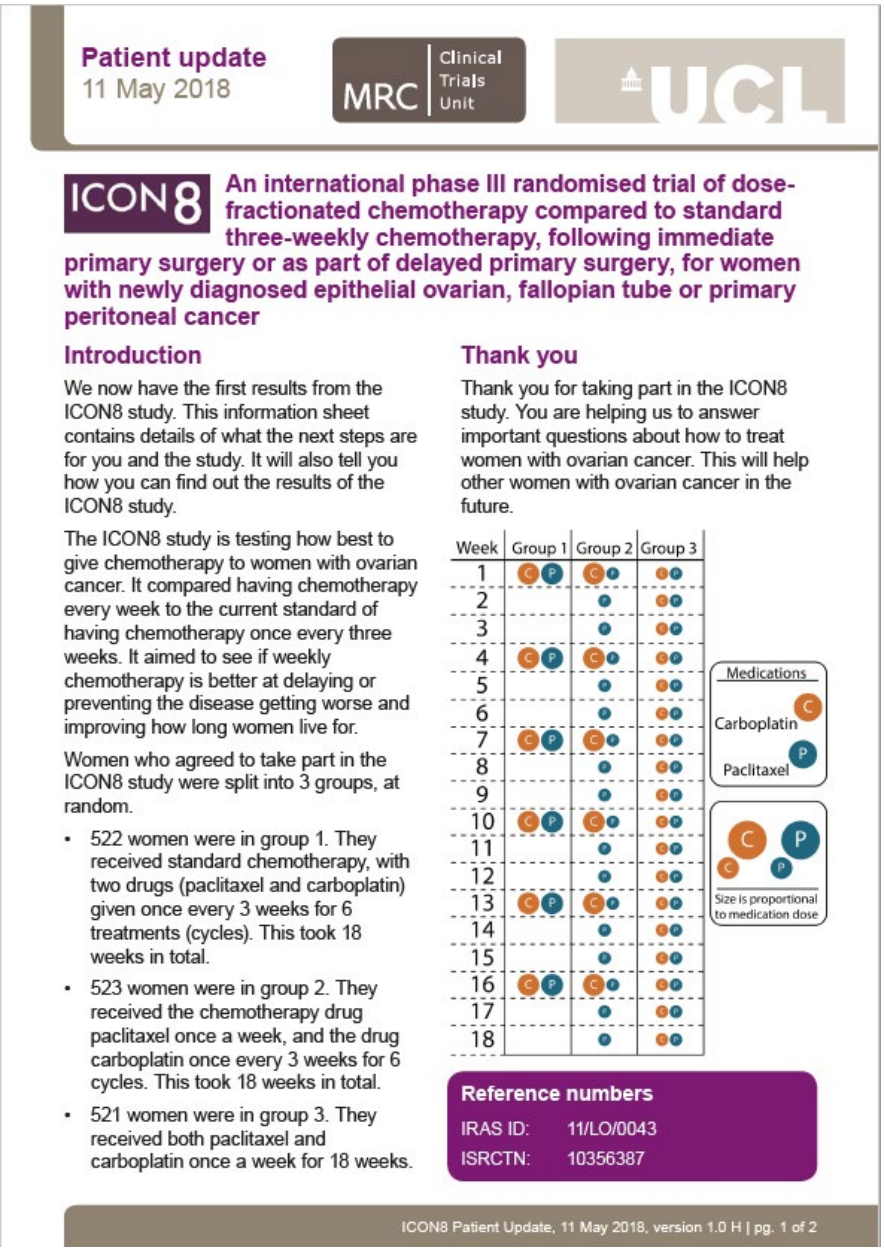
Patients described the Patient Update Information Sheet (Figure 8.2) as and Printed Summary (Figure 8.3) as well laid out and nice to look at. Some patients and site staff found the layout of the Basic Webpage (Figure 8.4) dull and would have preferred to have information conveyed in a more graphical way. Some site staff considered it less accessible than the other results summaries.

> *"I really like this [Printed Summary]. I think it's the layout as well … Visually, you can engage someone that's got an attention span of a two-year-old like me. You can immediately engage someone because of the way something is laid out; they're more likely to want to read it anyway." GMTCI02: Trial coordinator, medium site*

> *"This [Basic Webpage] looks the least attractive and least accessible to me." HLCLI02: Clinician, large site*

Most patients and site staff liked the look of the Enhanced Webpage (Figure 8.5), describing it as user-friendly, clear, and pleasing to look at. Participants generally said they liked the layout of the Email (Figure 8.6).

Figure 8.2: First page of the Patient Update Information Sheet



Patient update
11 May 2018

MRC Clinical Trials Unit

UCL

ICON8 An international phase III randomised trial of dose-fractionated chemotherapy compared to standard three-weekly chemotherapy, following immediate primary surgery or as part of delayed primary surgery, for women with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancer

Introduction

We now have the first results from the ICON8 study. This information sheet contains details of what the next steps are for you and the study. It will also tell you how you can find out the results of the ICON8 study.

The ICON8 study is testing how best to give chemotherapy to women with ovarian cancer. It compared having chemotherapy every week to the current standard of having chemotherapy once every three weeks. It aimed to see if weekly chemotherapy is better at delaying or preventing the disease getting worse and improving how long women live for.

Women who agreed to take part in the ICON8 study were split into 3 groups, at random.

- 522 women were in group 1. They received standard chemotherapy, with two drugs (paclitaxel and carboplatin) given once every 3 weeks for 6 treatments (cycles). This took 18 weeks in total.
- 523 women were in group 2. They received the chemotherapy drug paclitaxel once a week, and the drug carboplatin once every 3 weeks for 6 cycles. This took 18 weeks in total.
- 521 women were in group 3. They received both paclitaxel and carboplatin once a week for 18 weeks.

Thank you

Thank you for taking part in the ICON8 study. You are helping us to answer important questions about how to treat women with ovarian cancer. This will help other women with ovarian cancer in the future.

Week	Group 1	Group 2	Group 3
1	C P	C	
2			
3			
4	C P	C	
5			
6			
7	C P	C	
8			
9			
10	C P	C	
11			
12			
13	C P	C	
14			
15			
16	C P	C	
17			
18			

Medications
Carboplatin
Paclitaxel

Size is proportional to medication dose

Reference numbers
IRAS ID: 11/LO/0043
ISRCTN: 10356387

ICON8 Patient Update, 11 May 2018, version 1.0 H | pg. 1 of 2

8.4.1.2 Headings and broken-up text

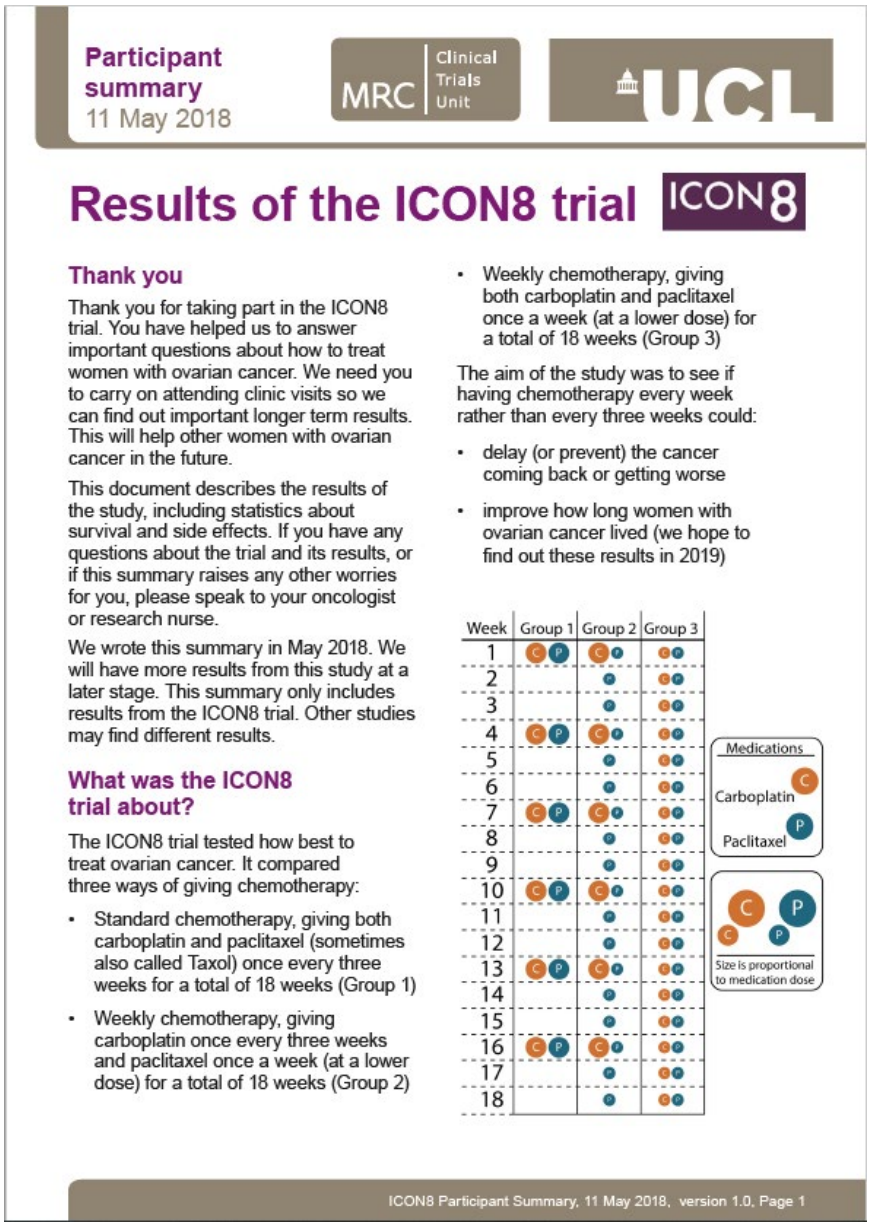
Patients and site staff appreciated the clear headings in all the interventions, which they said made it easy to find the information they were most interested in. Several patients also commented that they liked the text being broken up into small chunks.

> *"It's easy, in little chunks, because if I see messy, great big pieces I don't really want to be bothered, but if it's in nice chunks like this, that's how I like it." BMI01: Patient, medium site*

8.4.1.3 Use of columns

Some found the single column layout of the Basic Webpage easier to follow than the Enhanced Webpage, which used two columns, which some found distracting, or even messy and anxiety provoking.

Figure 8.3: First page of Printed Summary



Participant summary
11 May 2018

MRC Clinical Trials Unit

UCL

Results of the ICON8 trial

ICON8

Thank you

Thank you for taking part in the ICON8 trial. You have helped us to answer important questions about how to treat women with ovarian cancer. We need you to carry on attending clinic visits so we can find out important longer term results. This will help other women with ovarian cancer in the future.

This document describes the results of the study, including statistics about survival and side effects. If you have any questions about the trial and its results, or if this summary raises any other worries for you, please speak to your oncologist or research nurse.

We wrote this summary in May 2018. We will have more results from this study at a later stage. This summary only includes results from the ICON8 trial. Other studies may find different results.

What was the ICON8 trial about?

The ICON8 trial tested how best to treat ovarian cancer. It compared three ways of giving chemotherapy:

- Standard chemotherapy, giving both carboplatin and paclitaxel (sometimes also called Taxol) once every three weeks for a total of 18 weeks (Group 1)
- Weekly chemotherapy, giving carboplatin once every three weeks and paclitaxel once a week (at a lower dose) for a total of 18 weeks (Group 2)
- Weekly chemotherapy, giving both carboplatin and paclitaxel once a week (at a lower dose) for a total of 18 weeks (Group 3)

The aim of the study was to see if having chemotherapy every week rather than every three weeks could:

- delay (or prevent) the cancer coming back or getting worse
- improve how long women with ovarian cancer lived (we hope to find out these results in 2019)

ICON8 Participant Summary, 11 May 2018, version 1.0, Page 1

> *"I know this is the modern way to put stuff on, so that you have a column there and a column there, but I actually think this takes away from your concentration on what's this side." CSI01: Patient, small site*

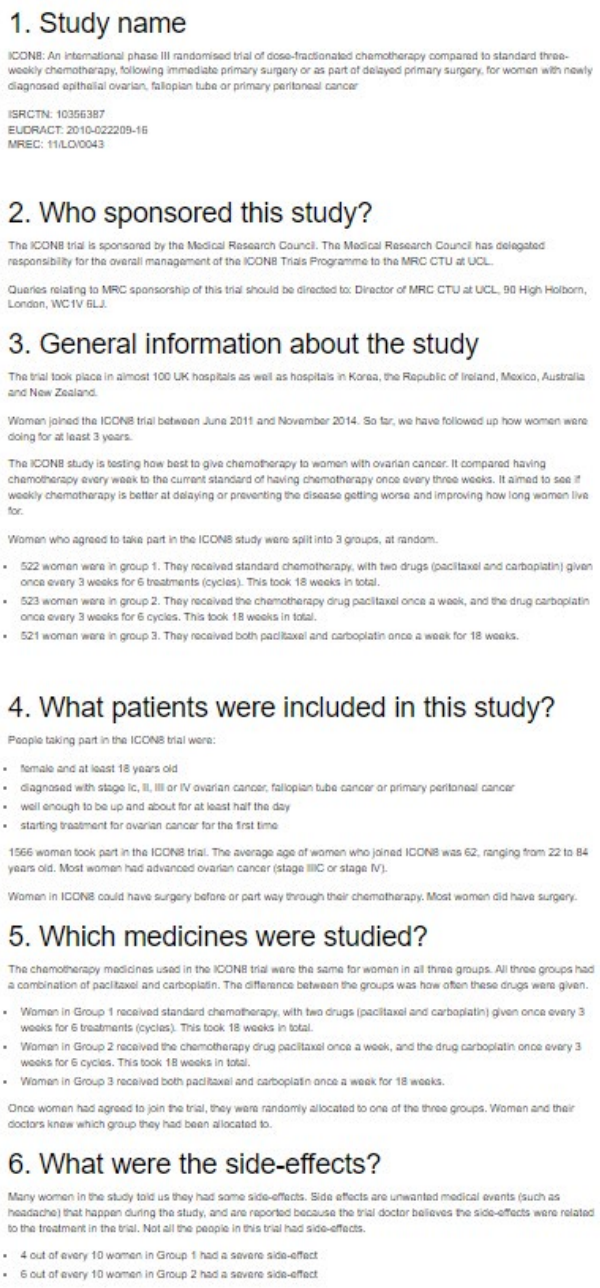
Site staff were divided about the layout of the Email, with some liking the simple one-column layout, while others described it as boring or bland. Although the content was essentially the same as the enhanced webpage, the visual appearance evoked different reactions.

> *"The email just looks bland, it looks boring compared. It's got exactly the same information on it, but it's just that the layout of it, I wouldn't recommend this" GMTCI02: Trial Coordinator, medium site*

8.4.1.4 Use of colour

The use of colour in the Printed Summary and Enhanced Webpage was appreciated by patients and site staff. The diagrams added colour to the

Figure 8.4: Extract from the body of the Basic Webpage



1. Study name

ICON8: An international phase III randomised trial of dose-fractionated chemotherapy compared to standard three-weekly chemotherapy, following immediate primary surgery or as part of delayed primary surgery, for women with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancer

ISRCTN: 10356387
EUDRACT: 2010-022209-16
MREC: 11/LO/0043

2. Who sponsored this study?

The ICON8 trial is sponsored by the Medical Research Council. The Medical Research Council has delegated responsibility for the overall management of the ICON8 Trials Programme to the MRC CTU at UCL.

Queries relating to MRC sponsorship of this trial should be directed to: Director of MRC CTU at UCL, 90 High Holborn, London, WC1V 6LJ.

3. General information about the study

The trial took place in almost 100 UK hospitals as well as hospitals in Korea, the Republic of Ireland, Mexico, Australia and New Zealand.

Women joined the ICON8 trial between June 2011 and November 2014. So far, we have followed up how women were doing for at least 3 years.

The ICON8 study is testing how best to give chemotherapy to women with ovarian cancer. It compared having chemotherapy every week to the current standard of having chemotherapy once every three weeks. It aimed to see if weekly chemotherapy is better at delaying or preventing the disease getting worse and improving how long women live for.

Women who agreed to take part in the ICON8 study were split into 3 groups, at random.

- 522 women were in group 1. They received standard chemotherapy, with two drugs (paclitaxel and carboplatin) given once every 3 weeks for 6 treatments (cycles). This took 18 weeks in total.
- 523 women were in group 2. They received the chemotherapy drug paclitaxel once a week, and the drug carboplatin once every 3 weeks for 6 cycles. This took 18 weeks in total.
- 521 women were in group 3. They received both paclitaxel and carboplatin once a week for 18 weeks.

4. What patients were included in this study?

People taking part in the ICON8 trial were:

- female and at least 18 years old
- diagnosed with stage Ic, II, III or IV ovarian cancer, fallopian tube cancer or primary peritoneal cancer
- well enough to be up and about for at least half the day
- starting treatment for ovarian cancer for the first time

1566 women took part in the ICON8 trial. The average age of women who joined ICON8 was 62, ranging from 22 to 84 years old. Most women had advanced ovarian cancer (stage IIIC or stage IV).

Women in ICON8 could have surgery before or part way through their chemotherapy. Most women did have surgery.

5. Which medicines were studied?

The chemotherapy medicines used in the ICON8 trial were the same for women in all three groups. All three groups had a combination of paclitaxel and carboplatin. The difference between the groups was how often these drugs were given.

- Women in Group 1 received standard chemotherapy, with two drugs (paclitaxel and carboplatin) given once every 3 weeks for 6 treatments (cycles). This took 18 weeks in total.
- Women in Group 2 received the chemotherapy drug paclitaxel once a week, and the drug carboplatin once every 3 weeks for 6 cycles. This took 18 weeks in total.
- Women in Group 3 received both paclitaxel and carboplatin once a week for 18 weeks.

Once women had agreed to join the trial, they were randomly allocated to one of the three groups. Women and their doctors knew which group they had been allocated to.

6. What were the side-effects?

Many women in the study told us they had some side-effects. Side effects are unwanted medical events (such as headache) that happen during the study, and are reported because the trial doctor believes the side-effects were related to the treatment in the trial. Not all the people in this trial had side-effects.

- 4 out of every 10 women in Group 1 had a severe side-effect
- 6 out of every 10 women in Group 2 had a severe side-effect

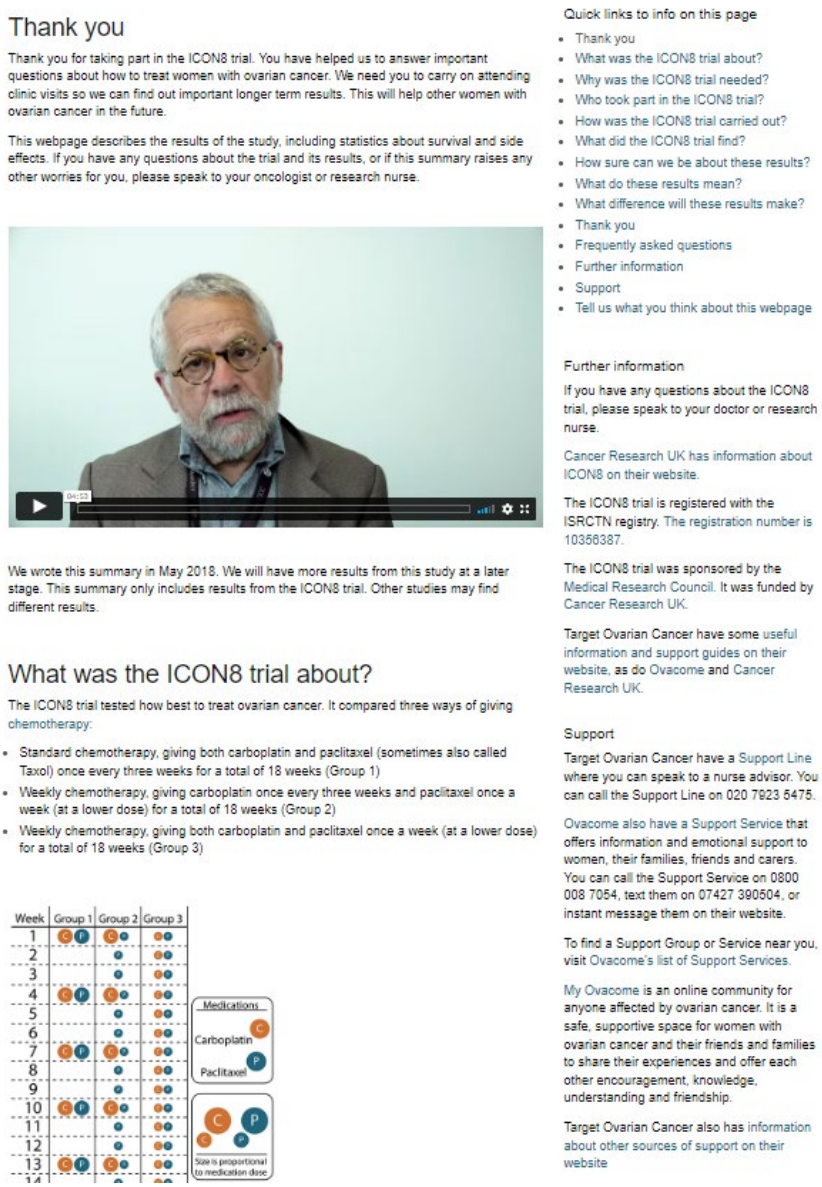
Enhanced Webpage that was missing from the Basic Webpage, which one patient said made the Enhanced Webpage more appealing to look at.

8.4.1.5 Structure

Some site staff felt that a summary of results and their implications could have been placed nearer the start of the summaries, to make it easier to find.

> *"I suppose the question is whether you have some sort of bullet-points about what the trial means for you and just generally close to the front of the information... a summary box upfront, so that presents that key information, hopefully will raise interest to make the patient, participant keener to read the full information summary." HLCLI02: Clinician, large site*

Figure 8.5: Extract from the body of the Enhanced Webpage



Thank you

Thank you for taking part in the ICON8 trial. You have helped us to answer important questions about how to treat women with ovarian cancer. We need you to carry on attending clinic visits so we can find out important longer term results. This will help other women with ovarian cancer in the future.

This webpage describes the results of the study, including statistics about survival and side effects. If you have any questions about the trial and its results, or if this summary raises any other worries for you, please speak to your oncologist or research nurse.

We wrote this summary in May 2018. We will have more results from this study at a later stage. This summary only includes results from the ICON8 trial. Other studies may find different results.

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The ICON8 trial tested how best to treat ovarian cancer. It compared three ways of giving chemotherapy:

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- Weekly chemotherapy, giving both carboplatin and paclitaxel once a week (at a lower dose) for a total of 18 weeks (Group 3)

Week | Group 1 | Group 2 | Group 3

Medications
Carboplatin
Paclitaxel
Size is proportional to medication dose

Quick links to info on this page

- Thank you
- What was the ICON8 trial about?
- Why was the ICON8 trial needed?
- Who took part in the ICON8 trial?
- How was the ICON8 trial carried out?
- What did the ICON8 trial find?
- How sure can we be about these results?
- What do these results mean?
- What difference will these results make?
- Thank you
- Frequently asked questions
- Further information
- Support
- Tell us what you think about this webpage

Further information

If you have any questions about the ICON8 trial, please speak to your doctor or research nurse.

Cancer Research UK has information about ICON8 on their website.

The ICON8 trial is registered with the ISRCTN registry. The registration number is 10356387.

The ICON8 trial was sponsored by the Medical Research Council. It was funded by Cancer Research UK.

Target Ovarian Cancer have some useful information and support guides on their website, as do Ovacome and Cancer Research UK.

Support

Target Ovarian Cancer have a Support Line where you can speak to a nurse advisor. You can call the Support Line on 020 7923 5475.

Ovacome also have a Support Service that offers information and emotional support to women, their families, friends and carers. You can call the Support Service on 0800 008 7054, text them on 07427 390504, or instant message them on their website.

To find a Support Group or Service near you, visit Ovacome's list of Support Services.

My Ovacome is an online community for anyone affected by ovarian cancer. It is a safe, supportive space for women with ovarian cancer and their friends and families to share their experiences and offer each other encouragement, knowledge, understanding and friendship.

Target Ovarian Cancer also has information about other sources of support on their website

For some patients, the structure of the information in the Basic Webpage was logical. However, some found it confusing, and gave up before reaching the results.

8.4.1.6 Navigation

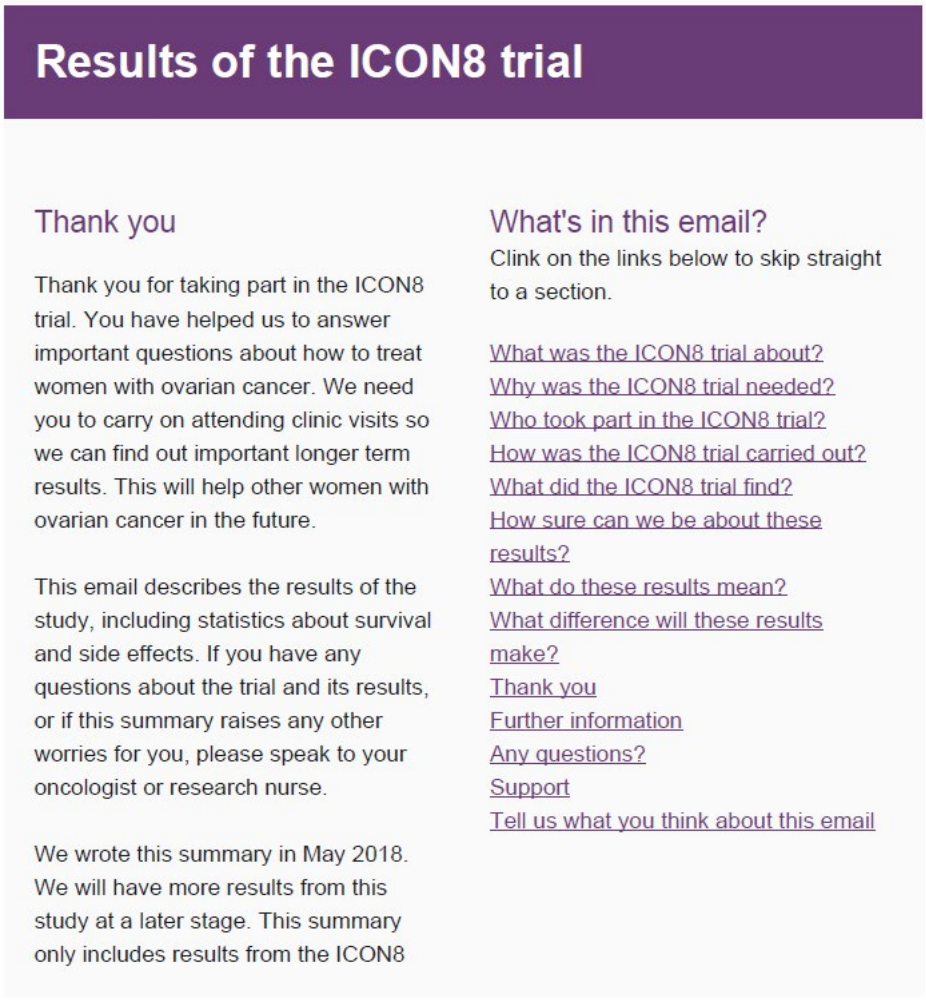
The Enhanced Webpage and Email contained 'quick links' at the top of the page (in the right hand column), so patients could navigate straight to any section they were interested in. The feature was appreciated by some.

> *"Having the quick links is quite good because you can jump to something and jump back to it." DLI01: Patient, large site*

8.4.1.7 Text size

Several people noted approvingly the large font size used for the Printed Summary and Patient Update Information Sheet.

Figure 8.6: Extract from the Email



Results of the ICON8 trial

Thank you

Thank you for taking part in the ICON8 trial. You have helped us to answer important questions about how to treat women with ovarian cancer. We need you to carry on attending clinic visits so we can find out important longer term results. This will help other women with ovarian cancer in the future.

This email describes the results of the study, including statistics about survival and side effects. If you have any questions about the trial and its results, or if this summary raises any other worries for you, please speak to your oncologist or research nurse.

We wrote this summary in May 2018. We will have more results from this study at a later stage. This summary only includes results from the ICON8

What's in this email?

Clink on the links below to skip straight to a section.

What was the ICON8 trial about?
Why was the ICON8 trial needed?
Who took part in the ICON8 trial?
How was the ICON8 trial carried out?
What did the ICON8 trial find?
How sure can we be about these results?
What do these results mean?
What difference will these results make?
Thank you
Further information
Any questions?
Support
Tell us what you think about this email

> *"I quite like the fact that it is slightly a larger font size, and I know that my husband would find it easier to read something like this than something with a smaller font." CSI01: Patient, small site*

There were mixed views on the font size of the Basic Webpage, which was slightly smaller than that used in the Enhanced Webpage. One patient who had viewed the Enhanced Webpage first, which uses larger type, asked if the basic webpage was meant for healthcare professionals because of the smaller type.

One research nurse was concerned about the use of bold for the average progression free survival times, worrying that it may draw too much attention to it.

8.4.1.8 Paper

One trial coordinator noted that the printed summary was printed on high quality paper, which was seen as a good thing.

> *"I particularly like the paper that the summary was printed on." FLTCI01: Trial Coordinator, large site*

8.4.2 Suggested adaptations to the Show RESPECT interventions

8.4.2.1 Suggested adaptations to the webpages

Some patients and site staff would have liked a webpage that contained some of the extra features of the Enhanced Webpage (video, FAQ section and links to support), while maintaining the single column layout of the Basic Webpage. Apart from the few patients who disliked the two-column layout, most patients had no suggestions for how to improve the Enhanced Webpage. There was a suggestion that the quick links might work better as a drop-down menu.

> *"Your quick links to info on this page, haven't you, on the side…? I just wondered whether it would work better with some sort of drop-down menu, so you have, under each section, you have a very short, bullet points summary? And then you can click on that to drop-down to more information? Just so it doesn't look quite so daunting when you open it for the first time." HLCLI02: Clinician, large site*

8.4.2.2 Suggested adaptations to the Printed Summary

Changes suggested for the Printed Summary included emphasising the key messages and thank you more visually, reducing the length of the printed summary, and using more bullet points.

> *"It's got the key sentence here, we think carboplatin and paclitaxel every three weeks should be the standard treatment. That should be in big letters, shouldn't it?" FLI01: Patient, large site*

One patient commented that she would prefer it if the Printed Summary had been broken up into more pages, with less information on each page, and use of pictures to make the text more attractive.

8.4.2.3 Suggested adaptations to the Email

The only suggestion for improvement for the Email was that women should be able to opt-in to the Email List when they joined the study, rather than when results were available.

8.4.3 Preferences between the interventions

Most patients and site staff preferred the Enhanced Webpage to the Basic Webpage, often giving multiple reasons for this. For some, this preference was, at least in part, due to the content items that the Basic Webpage lacked (FAQ section, diagrams, video, thanks). For some patients, the visual layout or navigability of the webpage was a reason for preferring it. Readability was another reason given for preferring it, as was it being more engaging or personal.

"It's quite user-friendly, it's got all the information that you need, it's easy for them to contact you should they need to, and the layout is really very good." GMTCI02: Trial Coordinator, medium site

A few patients and site staff preferred the Basic Webpage to the Enhanced Webpage. This was because they found the simpler, single-column layout of the Basic Webpage easier to navigate.

Many patients said they would prefer to receive results via the Printed Summary sent by post, rather than the webpages or Email. Table 8.1 summarises quantitative data on which interventions participants preferred, out of the ones they were offered. For some the reason for preferring the Printed Summary was the convenience of not having to access the webpage for themselves (particularly for those who were less confident with computers), and for others it was about having a physical copy they could read and file.

"It's just a physical thing isn't it, touching it and seeing it, being able to look back over it again. So, I think probably I would rather have a report, yes." BLI01: Patient, large site

Table 8.1: Patients' preferred intervention, from those they were offered[1]

	Preferred intervention		
Interventions offered	**Webpage n (%)**	**Printed Summary n (%)**	**Email list n (%)**
Basic Webpage & Printed Summary	2 (13)	13 (87)	
Basic Webpage & Email List	10 (63)		6 (34)
Basic Webpage, Printed Summary & Email List	1 (5)	17 (77)	4 (18)
Enhanced Webpage & Printed Summary	0 (0)	19 (100)	
Enhanced Webpage & Email List	6 (50)		6 (50)
Enhanced Webpage, Printed Summary & Email List	1 (4)	23 (88)	2 (8)

[1] NB participants offered only a webpage were not asked this question

Site staff also tended to prefer the Printed Summary as an approach for patients like those in ICON8, with or without a link to an Enhanced Webpage (Table 8.2) (the 'combination of approaches' described in the free-text of the questionnaire was almost always the Printed Summary plus Enhanced Webpage). This was often because they felt it would be more accessible for these patients.

"So personally I feel like the best method is to send it in the post, because not everyone has access to a computer, or has an email address or knows how to use a computer. And, you know, by sending it in the post you ensure that every participant who should receive it has received it." FLTCI01: Trial Coordinator, large site

There was considerable overlap in content between the Enhanced Webpage, Printed Summary and Email. For one patient, who had problems understanding

Table 8.2: Site staff's preferred method of communicating the results to participants

	Overall	Webpage			Posted Printed Summary (PPS)			Email List		
		Basic	Enhanced		No PPS	PPS		No Invitation	Invitation	
	n (%)	n (%)	n (%)	p-value	n (%)	n (%)	p-value	n (%)	n (%)	p-value
Posted Printed Summary	29 (43)	15 (43)	14 (42)	0.119	20 (61)	9 (26)	0.034	15 (43)	14 (42)	0.749
Email	1 (1)	1 (3)	0 (0)		1 (3)	0 (0)		1 (3)	0 (0)	
Basic Webpage	1 (1)	0 (0)	1 (3)		1 (3)	0 (0)		0 (0)	1 (3)	
Enhanced Webpage	6 (9)	0 (0)	6 (18)		1 (3)	5 (14)		3 (9)	3 (9)	
Combination of approaches	30 (44)	18 (51)	12 (36)		10 (30)	20 (57)		16 (46)	14 (42)	
Other	1 (1)	1 (3)	0 (0)		0 (0)	1 (3)		0 (0)	1 (3)	

the content, the mode in which it was delivered made little difference, as it did not address their main problems.

While many patients preferred to have a hard copy of the results, to enable them to keep it, and/or share with others easily, some who received the Printed Summary would have preferred to have looked up the results online. For other patients, the costs of posting and printing meant they would prefer to receive results in a way that was cheaper for the NHS.

8.5 Personalisation

In Show RESPECT site staff were asked to send the Patient Update Information Sheet (and Printed Summary, for those randomised to that intervention) by post. The protocol did not specify whether a personalised note or cover letter should be included. Some site staff chose to include a personalised note or cover letter along with the Patient Update Information Sheet / Printed Summary. The reasons given for this included:

- so patients were not alarmed
- so they knew whom to contact if they had any questions
- to explain what was included, and how it related to information they had previously been told
- to highlight that participants could opt out of receiving results (for sites randomised to the Printed Summary)

Some of the covering notes were the same for different patients, whereas others were tailored individually. This personalisation did take additional time, but some site staff felt strongly that they should not send the results out without the personal note, coming as it did in the context of a relationship with patients that had often been developed over several years. This was appreciated by some patients, making them feel more valued. Individual emails were another way suggested by a patient of communicating the results more personally.

Not all sites included personalised notes or cover letters alongside the Patient Update Information Sheet or Printed Summary. Some did not think it was needed because the Patient Update Information Sheet contained all the necessary information. Others felt they did not know participants well enough to write a properly personalised note.

> *"I sent it by itself, but just because I didn't know the patients. I want a cover letter to be quite personal, and so I wasn't comfortable writing a cover letter to patients I didn't particularly know. And then I didn't want it to be generic, I feel like they probably deserve a bit more than that. I do understand that they probably deserve more than just a piece of paper*

saying here's an update sheet, but I just didn't know how to do the in-between of personal but generic." CLTCI04: Trial Coordinator, large site

Some of the communication approaches used in Show RESPECT were seen as more personal than others. For example, one patient talked about receiving an email feeling more personal than reading the same information on a webpage. Another patient said that the Enhanced Webpage felt more personal than the Basic Webpage, because of the thank you message and video.

8.6 Opt-in versus opt-out approaches to sharing results

To access the results via a webpage or email, patients had to take action themselves (visit a URL), so these approaches were opt-in. However, the Printed Summary was sent on an opt-out basis; patients had to let their site staff know if they did not want to receive the results. Only three participants opted out of receiving the ICON8 results by Printed Summary. This creates the possibility that some patients who did not want to find out the results may have been exposed to them if they had not spotted the information about opting out. The quantitative results of Show RESPECT suggest that this did not happen (at least for patients who responded) (Section 5.2.5).

Patients, including those who did not want to receive the results, viewed the opt-out approach as good, offering people the results but giving them the chance to decline. However, one patient was concerned about the possibility of results being sent to patients who were too ill to opt out.

"I think you should be offered postal, but then opt-out if you're okay not getting postal. I think that's the best way to go." GMI02: Patient, medium site

One patient commented that opting-in to the email list should happen at the point people join the trial, rather than at the end.

Staff at some large sites, who had found sending printed summaries to all participants who did not opt-out time-consuming, would have preferred an opt-in approach to reduce the workload. One research nurse thought that handling opt-ins may be challenging for studies with large numbers of participants, even though it was a good idea in principle. However, other research nurses said they were used to keeping track of information like that, so it would not be a problem. Collecting opt-ins at the time of gaining informed consent to join the study might be a practical way of implementing the approach, although some patients may change their minds in the interim.

Other site staff felt the opt-out approach was good, enabling patients to choose whether or not to receive the results. It was felt that patients who don't want results are more likely to opt-out than patients who do want results are

to opt-in. Some highlighted the option of opting out in a compliments slips or cover letter that went with the Patient Update Information Sheet, to make sure patients did not miss that information, while others talked to participants on the telephone to make sure they were aware.

> *"I think they just wouldn't care enough to call to opt in, whereas if they really didn't want the results then I think they'd be more willing to call or take the time out of their day to do that." CLTCI04: Trial Coordinator, large site*

8.7 Discussion

8.7.1 Summary of key findings

For patient populations like those who took part in ICON8 (mostly women aged 60 or over), Posted Printed Summaries of results were generally preferred by patients and site staff. This preference was partly related to the accessibility of the approach, compared to email or webpages, in the context of 4 in 10 ICON8 participants not using email or the internet every day. Posted Printed Summaries also facilitated the filing of information for future reference, and sharing with friends and family members. Some of the features of the Enhanced Webpage (the short video, links for further information and support, and the FAQ section) were seen as being potentially useful for some participants, leading some site staff to advocate for a combination of the Posted Printed Summary and Enhanced Webpage.

The information contained in the results summaries tested in Show RESPECT generally covered the topics that patients were interested in and was written in a way most participants could understand. While some patients identified further information they would like, this should be balanced against the need to keep summaries concise. There was no consensus around what, if anything, was missing, suggesting the content included was a good basis, if patients are provided with ways to seek additional information if required. The layout of the interventions was generally liked, with large text size, use of colour, clear headings and broken-up text all contributing to the ease of use and attractiveness of the interventions.

Trial results come to patients in the context of relationships with site staff developed over the course of trial participation, which, in the case of ICON8, was several years. In this context, some site staff were keen to personalise the results communication in some way, through adding covering letters or compliments slips with short notes, or phoning participants before or after sending out the results. This was appreciated by some participants, making them feel valued. However, it may not be necessary where patients do not

have such close relationships with site staff (for example, if their research nurse has changed several times over the course of a trial). Some patients would have preferred more personal communication of the trial results (for example, through a face-to-face conversation), however, there was generally an awareness of the resource constraints of the NHS, and most patients were pleased to receive the results through the approaches used in Show RESPECT.

8.7.2 Strengths of this study

The qualitative interviews with patients and site staff allowed me to collect detailed feedback on the interventions used within Show RESPECT. After describing their memories of their initial thoughts about the interventions they actually received, participants were asked to 'think aloud'[112] while looking at each Show RESPECT intervention in turn. This means I have data from nearly all interviewees (patients and site staff) on all the interventions, rather than just the ones their site was randomised to, or they chose to use, giving me a rich dataset.

Triangulating data from site staff and patients, and from interviews and questionnaires, gives me breadth in the range of respondents I have data from, and depth. Many of the free-text responses were surprisingly rich, complementing the data from interviewees.

8.7.3 Limitations of this study

One challenge in collecting qualitative data around the Show RESPECT interventions was minimising the impact of social desirability bias, particularly as site staff were aware of my role as Chief Investigator in the study. There was a danger that this may have meant they would be reluctant to criticise the interventions for fear of offending or upsetting me. I tried to minimise this risk through explicitly asking about whether there was anything they disliked, trying to create a comfortable atmosphere in the interviews, and give visual and verbal cues that indicated interest but not a particular emotion. With patients, I purposely did not explain my role in developing the interventions, to reduce this risk. Encouraging interviewees to make comparisons between the interventions (and any other previous experience they had of sharing/receiving trial results) gave a non-confrontational way for interviewees to highlight weaknesses of specific interventions through contrasting it with things they preferred, allowing them to frame things positively. Together, these approaches seem to have allowed both patients and site staff to express criticism of the interventions, but I cannot rule out some having filtered their comments so as not to cause offense.

As discussed in Section 7.11.3, Show RESPECT was conducted within the context of a single clinical trial, meaning care is needed transferring findings to other trials.

8.7.4 Conclusions

Posted Printed Summaries were preferred by patients and site staff compared to electronic methods of sharing results, as they were seen as accessible to everyone, and easy to keep and share with others. At the same time, some of the features of the Enhanced Webpage (video, links to further information and support, and Frequently Asked Questions section) may be useful for some participants, suggesting offering participants both may be a good approach for sharing results.

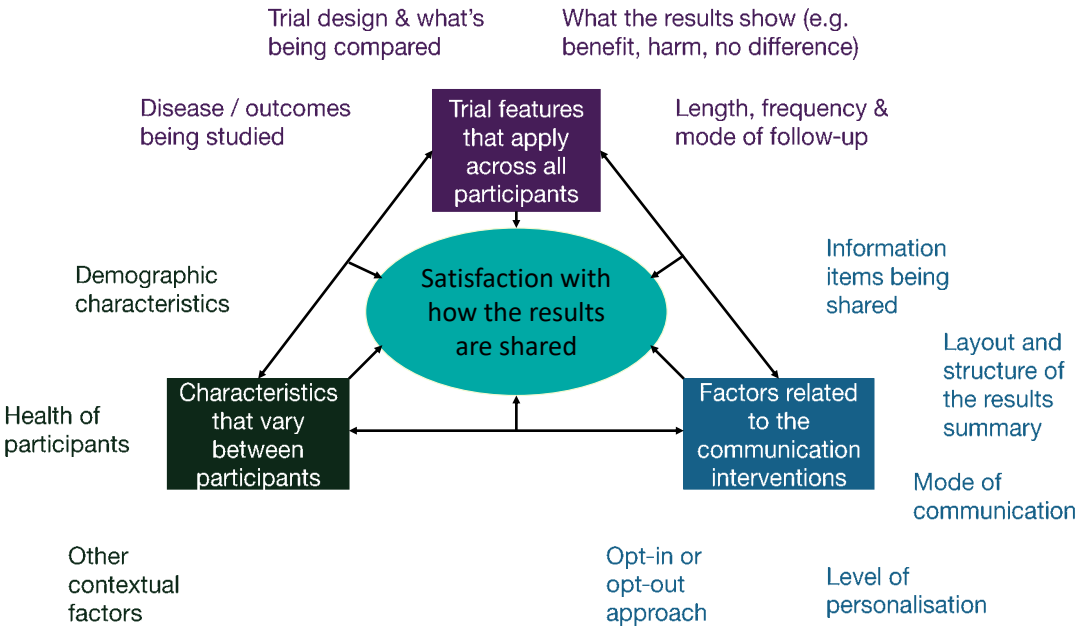
However, the Show RESPECT interventions themselves may not have been the only factors that influenced participant satisfaction with how the results were shared. The next chapter explores what other factors may influence participant satisfaction, including participant characteristics such as age, education level and health, and trial factors such as the disease area, what the results show, and what the trial is comparing.

9. What other factors influence satisfaction with how the results were shared?

9.1 Overview of the scope of this chapter

Satisfaction with how trial results are shared is influenced by a complex interplay between factors related to the trial itself, the characteristics of individual participants and the aspects of the mode of communication discussed in Chapter 8. This chapter explores those features that apply to all participants, and the characteristics that vary between participants, that affect satisfaction with how the results are shared, using qualitative and quantitative data from patients and site staff. Table 9.1 summarises the factors explored in this chapter, and Figure 9.1 illustrates how these factors interact with each other and factors related to the communication approach. When planning how to share results with participants, and developing communication tools, trialists will know about the features that apply to all participants (shown in the first row of Table 9.1). However, they also need to take into account that the characteristics outlined in the second row will also influence satisfaction with how the results are shared (and may not all be known to those sharing results). Understanding what these factors are, and their impact on satisfaction, may be helpful when thinking about how transferable or generalisable the Show RESPECT findings are to other studies with different trial and patient characteristics. The chapter concludes with a short discussion of the key findings, strengths and limitations of this study.

Figure 9.1: Summary of factors that influence participant satisfaction with how trial results are shared



Chapter 9 Summary Box

Why was this study done?

- Understanding how trial and patient characteristics affect satisfaction with how the results are shared may help researchers think about the generalisability or transferability of the Show RESPECT results to other trials, and identify what they need to consider when planning to communicate the results from future trials.

What did I do?

- I analysed questionnaire and interview data from patients and site staff relating to how trial and individual-level factors may have influenced patients' satisfaction with how trial results were shared within the Show RESPECT study.

What did I find out?

- The ICON8 trial found that weekly chemotherapy was not better than three-weekly chemotherapy; in some ways **this made the results easier to receive for patients in the control arm** as no-one had missed out on a superior treatment.
- **Communication of results takes place within the context of relationships that have developed over the course of the trial** between patients and site staff; in the case of some patients and site staff, these relationships were close, creating a desire for more personal communication of trial results
- **Patients across all ages, education levels and computer competencies were more likely to be satisfied with how the results were shared if they received the Posted Printed Summary.** This suggests that the higher levels of satisfaction from the Posted Printed Summaries were not solely due to the patient population in ICON8 being older and less comfortable using computers.

What do these findings mean?

- Trials that find clear differences between the arms may need to communicate results to people in the group that did less well overall in a more personal way, or offer further support to these people.
- Communication of trial results should take into account the strength of relationships developed between site staff and patients, for example, allowing a degree of personalisation of how the results are shared where these relationships are close.
- Posted Printed Summaries seemed to benefit all patients, not just those who used email or internet less than daily.

Table 9.1: Overview of factors explored in this chapter

		Section
Trial features that apply across all participants within a trial	Disease area	9.2.1
	Trial design, interventions and control	9.2.2
	What the trial results show	9.2.3
Characteristics that vary between participants within a trial	Demographic characteristics of participants (e.g. age, education level, sex)	9.3.1
	Randomised arm	9.3.2.1
	Participants' health at time of receiving results	9.3.2.2
	Participants' experience of trial interventions (e.g. side-effects)	9.3.2.3
	Relationship with trial staff	9.3.3.1
	Understanding of the trial	9.3.3.2
	Expectations around receiving results and what they will show	9.3.3.3
	Access to support	9.3.3.4

9.2 Features that apply across all participants within a trial

I found several features that apply across all participants within a trial that may have some influence on how the overall trial results are received, and satisfaction with how they are shared. These include disease area, comparator, and what the results showed. Section 2.3.2 describes the ICON8 trial, which is the context in which Show RESPECT took place.

9.2.1 Disease area and outcomes of interest

Ovarian cancer is a serious condition, often with a poor prognosis (see Section 2.4.1). The ICON8 trial aimed to improve progression free survival (the time until the disease gets worse or the patient dies) and overall survival. This means participants had a lot riding on the success of the trial.

One participant who did not want to find out the trial results for ICON8 said she would have wanted to find out the results if she had been taking part in a trial for a less serious condition.

> *IV: If it had been a trial looking at how to treat your heel problems, that might have been different?"*
>
> *GSI01: "Oh, that's fine because it's a heel, I wasn't going to die of that. It might have been a nuisance, I might have moaned about it a huge amount, but that was a different matter; that wasn't life or death." GSI01: Patient, small site, did not want to receive results*

Site staff felt that the severity of the disease, and survival being an outcome, meant that extra care needed to be taken when sharing results. By the time the first results were available a substantial number of participants had died. Show RESPECT was looking at communication of results to participants who were alive at the time results were available, but the ICON8 results inevitably reflect that some participants were not so fortunate. Site staff felt this may be sobering or upsetting to some patients.

> *"If you were alive, you read the results, and there was a high mortality rate, I don't know how that would make me feel. Depressed, and grateful that I was still there to read the results" GMTCI02: Trial Coordinator, medium site*

However, the severity of the disease may not necessarily make a difference to how results should be communicated, if participants are aware of their prognosis at the time they join the trial. The patients I interviewed did seem aware of the severity of ovarian cancer, although some sought to avoid information on this in order to protect themselves, and one clinician described this understanding as something that grows over time, rather than necessarily being fully understood at the point of diagnosis, when they are invited to join the trial.

> *"Because most of these patients, when they were recruited into the study, they know and they were told that some of them will be stage IIIc ovarian cancer, which they know how bad their chances are. So no, I don't think it affects that. They sort of understand. Patients understand, especially how far their stage is and what it involves." BMRNI04: Research nurse, medium site*

9.2.2 Trial design, intervention(s) and control

ICON8 was an open-label Phase III trial comparing different dosing schedules for standard chemotherapy drugs, rather than testing a new drug. Many patients saw the trial as low-risk when they joined, as the chemotherapy drugs being used were well established, with only the frequency and dose varying between arms. Placebo-controlled trials were seen to raise more complex issues around communication of results, such as the practicalities of unblinding, and some participants not having received an active treatment. Sites and participants do not always find out which arm participants had been randomised to in placebo-controlled trials, and if they do it is often long after the trial has finished. Patients may have wanted to find out the results more personally, through a conversation with their doctor, had the trial been placebo controlled. Site staff felt that earlier phase trials might raise different issues to Phase III trials, and it may not always be appropriate to share results with participants in early phase trials, as results may be harder for patients to interpret as these trials do not focus efficacy. Another type of trial where

site staff felt it might be more difficult to share results is in trials in emergency settings, where patients are not asked for informed consent prior to being randomised.

9.2.3 What the trial results showed

ICON8 found no difference between the three arms, in terms of progression-free survival, with little difference in side-effects. As such, there were no clear 'winners' or 'losers' from taking part in the trial. This may make receiving the results a less emotionally intense experience for participants. Some trial results may also be harder to understand than others (e.g. where the results are uncertain, or when the effect of an intervention varies by sub-groups).

Doctors may be more keen to share results with participants if the results are seen as 'good'. Sharing results may be more difficult in certain result scenarios (for example if the intervention caused harm). This was not seen as a reason not to share results, but needs to be taken into account when deciding how to share results.

> *"I think, when there's some really good results a doctor always feels that's what they want to tell their patients. Whereas if there's a marginal benefit, then you're likely to not really want to say too much of the results." EBLMCLI02: Clinician, large and medium sites*

Some women felt that their emotional response would have been different, had the results showed a difference between the arms. Patients speculated that they may have felt angry or upset if their treatment arm turned out to be less good, but the extent of this may depend on their own health at the time of receiving results, as well as the results for the group overall. Some participants and site staff felt that if the results had been different (complex or potentially upsetting), it may be better to communicate them in a different way, with more personal approaches generally being preferred, giving patients more support to process that information, while some patients would want less information. Site staff felt it was important to know what arm a participant was on before telling them the results, if there was a difference between the arms, in order to share the results carefully and sensitively.

> *"It would depend if it raised more questions perhaps. So maybe a clinician would have been better suited I suppose, if it was going to have that effect. Maybe the clinician giving a paper and discussing it in clinic maybe better for them than obviously reading it at home on their own." GSTCI03: Trial coordinator, small site*

> *"If it went into my head that I was going to see more bad news about my participating group I might be less inclined to want to see a written report and just a referral to a website. Because this is almost... When you receive this [printed summary] you have to look at it whereas with the website you may think, oh, I'm not going to bother. You can ignore it more easily if you*

feel that your group is not going to have any more good news or better results." BLI01: Patient, large site

However, not all patients and site staff felt that, had the results been different, they would have wanted to receive/share the results in a different way. One patient, whose disease had progressed, talked about it not mattering to her too much, as she had made the decision to join the trial in the knowledge that it might help her, but it might not. She preferred not to dwell too much on what might have been, focusing instead on the future. While how the results are shared may not need to change, depending on the results, the way it is written needs to be carefully thought through.

"It would be the same. Of course, maybe if they had been in an arm which had been very inferior, very different, you would feel a little bit disappointed for them especially if the cancer is coming back. You know? But I mean... I don't think there would be a difference really. Because what is done has been done. You can't undo it." BMRNI04: Research nurse, medium site

While some site staff would want to give the results face-to-face in clinic, patients may require more time and privacy for processing potentially distressing information, if they were on the worse arm, which the clinic setting may not necessarily offer. This led other site staff to prefer giving patients the information to access in their own time and space, via a webpage or printed summary, with the offer of further support if needed.

"I think if the results had been bad (in terms of I would have had to tell them that this treatment arm is better than your treatment arm), I think how they react to that, the clinic isn't as private as you would want. If I had to tell them to their face I don't think it would have been as good as me just sending them something on the web page and then putting at the bottom, you know, they needed any further support or whatever they can just call me. Instead of having them be in front of everyone reacting to it, be able to read it on their own time in their own space and react how they would want to react." CLTCI04: Trial Coordinator, large site

9.3 Characteristics that vary between participants

It is important to remember that every trial participant is unique, even within trials with narrow inclusion and exclusion criteria. I looked at the qualitative and quantitative data on characteristics that vary between participants that could make a difference to their experience of receiving trial results. These factors included demographic characteristics (age, education level and how frequently they use the internet or email). I examined factors related to their health (which arm of the ICON8 trial they were randomised to, whether they had experienced disease progression by the time they received results, and the side-effects they experienced when taking part in the trial). I also looked at their relationship

with site staff, understanding of the trial and its potential outcomes, their expectations around receiving results, and the support they had access to in terms of family, friends and support groups.

9.3.1 Demographic factors

I carried out pre-specified sub-group analysis to explore if the effect of any of the Show RESPECT interventions on reported satisfaction with how the results were shared differed by age, ICON8 arm, education level and reported frequency of internet/email use. The results of this sub-group analysis can be found in Table 9.2 and Figure 9.2. Particular attention should be given to the results of the interaction tests (shaded pink), as these test whether there was evidence that the effect of the intervention differed by sub-group[113, 114]. Differences between the subgroups were nearly all quantitative rather than qualitative, i.e. the direction of effect was the same, just the magnitude of effect seemed to differ, and the interaction tests showed no evidence of heterogeneity of effect by any of the subgroups tested. As Figure 9.2 shows, the confidence intervals for the individual subgroups are often wide, and the trial was not powered to detect sub-group effects, and so caution is needed in interpreting these results. I was unable to test for heterogeneity by whether their first language was English as so few respondents reported English not being their first language.

Figure 9.2: Forest plot showing the adjusted odds ratio for satisfaction with how the results were shared for each of the three randomisations, by sub-group

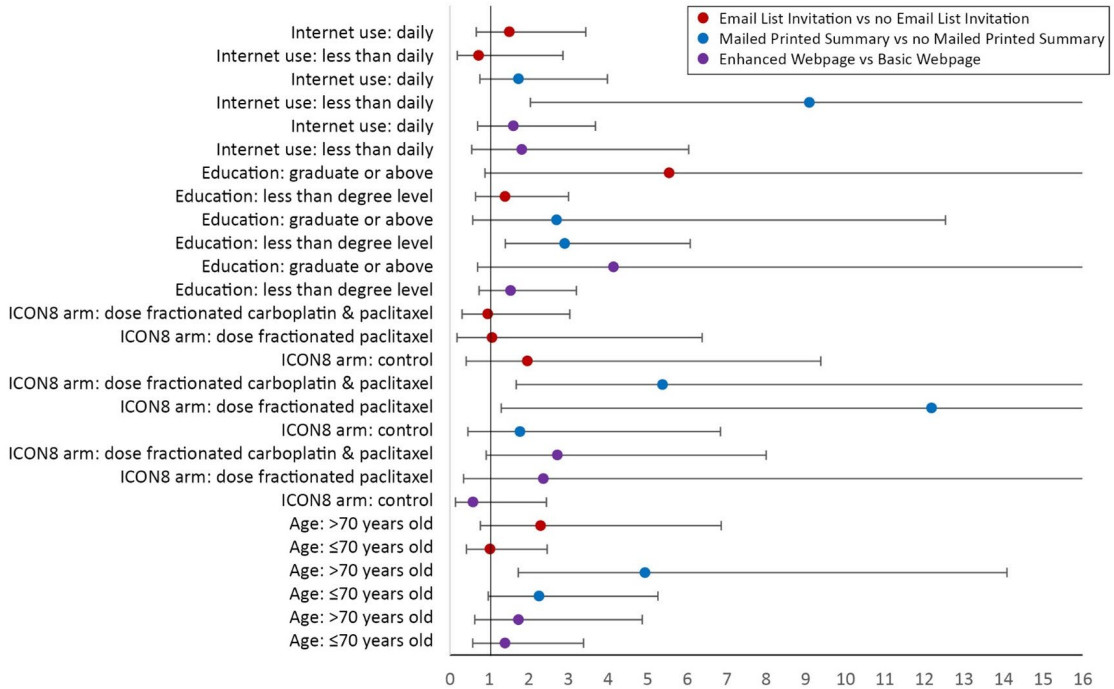


Table 9.2: Subgroup analyses for individual-level factors that may affect satisfaction with how the results were shared

	Very unsatisfied n (%)	Quite unsatisfied n (%)	Neither satisfied nor unsatisfied n (%)	Quite satisfied n (%)	Very satisfied n (%)	Unadjusted ordinal odds ratio[1] (95% CI) p-value			Adjusted ordinal odds ratio[2] (95% CI) p-value		
						Enhanced vs basic webpage	Printed summary (PS) vs no PS	Email list vs no email list	Enhanced vs basic webpage	Printed summary (PS) vs no PS	Email list vs no email list
Age							**Interaction test:**		p=0.654	p=0.112	p=0.926
≤70 years old	8 (9)	5 (6)	9 (11)	25 (29)	38 (45)	1.39 (0.61 to 3.19) p=0.437	2.66 (1.17 to 6.04) p=0.019	0.84 (0.36 to 1.94) p=0.686	1.40 (0.58 to 3.38) p=0.447	2.26 (0.97 to 5.26) p=0.059	1.02 (0.42 to 2.46) p=0.970
>70 years old	4 (7)	7 (12)	8 (13)	15 (25)	26 (43)	1.48 (0.56 to 3.93) p=0.428	4.69 (1.66 to 13.20) p=0.003	2.59 (0.89 to 7.51) p=0.079	1.74 (0.63 to 4.86) p=0.286	4.94 (1.73 to 14.09) p=0.003	2.30 (0.77 to 6.86) p=0.136
Arm in ICON8 trial							**Interaction test:**		p=0.424	p=0.543	p=0.557
Standard treatment	3 (8)	2 (5)	5 (13)	10 (26)	18 (47)	0.86 (0.24 to 3.11) p=0.823	1.76 (0.48 to 6.44) p=0.396	2.34 (0.62 to 8.87) p=0.209	0.59 (0.14 to 2.44) p=0.467	1.78 (0.46 to 6.84) p=0.403	1.96 (0.41 to 9.38) p=0.399
Dose fractionated paclitaxel	4 (8)	4 (8)	7 (13)	13 (25)	24 (46)	2.22 (0.32 to 15.37) p=0.417	10.35 (1.29 to 83.07) p=0.028	1.22 (0.21 to 7.11) p=0.826	2.37 (0.35 to 16.20) p=0.380	12.18 (1.30 to 114.21) p=0.029	1.07 (0.18 to 6.38) p=0.942
Dose fractionated carboplatin & paclitaxel	5 (9)	6 (11)	5 (9)	17 (31)	22 (40)	2.47 (0.86 to 7.06) p=0.092	5.51 (1.77 to 17.08) p=0.003	0.91 (0.31 to 2.68) p=0.862	2.72 (0.92 to 8.00) p=0.069	5.38 (1.68 to 17.28) p=0.005	0.96 (0.31 to 3.03) p=0.949

	Very unsatisfied n (%)	Quite unsatisfied n (%)	Neither satisfied nor unsatisfied n (%)	Quite satisfied n (%)	Very satisfied n (%)	Unadjusted ordinal odds ratio[1] (95% CI) p-value			Adjusted ordinal odds ratio[2] (95% CI) p-value		
						Enhanced vs basic webpage	Printed summary (PS) vs no PS	Email list vs no email list	Enhanced vs basic webpage	Printed summary (PS) vs no PS	Email list vs no email list
First language											
Not English	0 (0)	0 (0)	0 (0)	3 (75)	1 (25)						
English	12 (9)	12 (9)	16 (12)	37 (27(	62 (45)						
Education							**Interaction test:**		p=0.520	p=0.930	p=0.951
Less than degree level	10 (9)	10 (9)	14 (13)	23 (21)	51 (47)	1.47 (0.71 to 3.04) p=0.297	2.92 (1.40 to 6.08) p=0.004	1.39 (0.67 to 2.93) p=0.378	1.54 (0.74 to 3.20) p=0.252	2.91 (1.40 to 6.08) p=0.004	1.40 (0.65 to 3.00) p=0.388
Graduate or above	2 (5)	2 (5)	3 (8)	17 (28)	13 (35)	2.20 (0.48 to 10.20) p=0.313	5.01 (1.19 to 21.06) p=0.028	1.89 (0.46 to 7.79) p=0.377	4.14 (0.70 to 24.60) p=0.118	2.70 (0.58 to 12.53) p=0.204	5.55 (0.89 to 34.40) p=0.066
Reported internet/email use							**Interaction test:**		p=0.955	p=0.104	p=0.662
Less than daily	4 (7)	6 (11)	7 (13)	17 (31)	21 (38)	1.83 (0.56 to 5.95) p=0.317	8.18 (1.93 to 34.71) p=0.004	0.87 (0.23 to 3.21) p=0.829	1.82 (0.55 to 6.04) p=0.331	9.09 (2.04 to 40.42) p=0.004	0.73 (0.19 to 2.86) p=0.653
Daily	8 (9)	6 (7)	10 (11)	22 (25)	43 (48)	1.65 (0.73 to 3.75) p=0.232	1.82 (0.80 to 4.14) p=0.151	1.42 (0.64 to 3.16) p=0.393	1.61 (0.70 to 3.68) p=0.259	1.74 (0.76 to 3.98) p=0.189	1.51 (0.67 to 3.44) p=0.321

[1] Adjusted for strata, randomisation phase (early vs late) and clustering

[2] Adjusted for the other factors reported in this table (except first language) as well as strata, randomisation phase (early vs late) and clustering

9.3.1.1 Does patients' age make a difference to satisfaction with how the results were communicated?

Patients of all ages seemed to benefit from having a Printed Summary sent to them by post, rather than having to access the results via a webpage or Email. I found no strong evidence that older patients benefited more than younger patients from the Printed Summary in the sub-group analysis (interaction test p=0.112) (Table 9.2 and Figure 9.2), although the point estimate for the adjusted ordinal odds ratio was larger in the older sub-group (4.94 for women aged >70 years, and 2.26 for those aged 70 or younger). Similarly, there was no strong evidence of heterogeneity of effect in the Webpage or Email List randomisations (interaction test enhanced vs basic webpage p=0.654, email list invitation vs no invitation p=0.926). In contrast, site staff felt that the age of participants would affect how they would prefer to receive the results. They hypothesised that older patients would prefer Printed Summaries, while younger patients may be happier with webpages or Emails. This distinction may reduce over time, as people who are familiar with computers and the internet get older.

> *"I think you've got to look at the age group of the patients. I think that is the main thing. You've got to look at the age group of the patient. So everybody is individual, so like, if you are looking at maybe 65 and above, they would mostly prefer written summaries. Whereas the younger group will want the website." BMRNI04 – Research Nurse, medium site*

9.3.1.2 Does education level make a difference to satisfaction with how the results were communicated?

The women I interviewed who did not have at least A level qualifications seemed less satisfied, struggling to understand the results, or to access them. This is supported by the results shown in the left half of Table 9.2, with 18% of those educated to less than degree level being very or quite unsatisfied, compared to 10% of graduates. Some site staff felt that more educated participants may want more detail than participants with fewer qualifications, however from the participant interviews this was not necessarily the case, with some highly educated participants wanting only headline results, while others wanted a lot of detail.

As with age, patients of all education levels seemed to benefit from the Printed Summary, with the point estimates for the ordinal odds ratio being very similar (less than degree level: 2.91, graduate or above: 2.70, interaction test p=0.930) (Table 9.2 and Figure 9.2). There was also no good evidence of a difference of effect of the Enhanced Webpage (interaction test p=0.520) or Email List Invitation (interaction test p=0.951) by education level. While the point estimate

for the email list invitation is large for the graduate or above subgroup, it is very likely that this is due to chance, given no participants signed up to the email list. As discussed in Section 8.3.10, patients and site staff felt the video that was contained in the Enhanced Webpage could be useful for patients who were less comfortable with reading, but there is no evidence from the quantitative data that those with lower levels of qualifications benefited more from the Enhanced Webpage. It may have been that participants who struggle with literacy have developed alternative coping strategies for these sorts of occasions. One research nurse described a patient asking her to read the results to her, as she said she had forgotten her glasses. However, the nurse suspected that it was because she could not read, but did not want to admit it.

9.3.1.3 Does frequency of internet and email use make a difference to satisfaction with how the results were communicated?

Patients' level of satisfaction with how the results were shared overall did not appear to be affected by frequency of internet/email use in the quantitative analysis, as shown in the left hand portion of Table 9.2. There was no good evidence of frequency of internet/email use interacting with the effect of any of the interventions, with the interaction tests for the Enhanced Webpage vs Basic Webpage, Printed Summary vs No Printed Summary, and Email List Invitation vs No Invitation being p=0.955, p=0.104 and p=0.662 respectively. The point estimate for the ordinal odds ratio of the Printed Summary was much higher in the group who used the internet/email less than daily (9.09, compared to 1.74), however the direction of effect was the same across both sub-groups, and the confidence intervals were wide. In the qualitative interviews, participants' frequency of using email/internet did not seem to affect satisfaction. Some participants with lower computer literacy got the help of family members to access results (or asked site staff for printed copies), which may have mitigated the challenges for those who were randomised to no printed summary. Similarly, as reported in Chapter 5, patients' views on whether the results were easy to access did not vary by randomisation, suggesting online approaches were not inaccessible to most people. However, many site staff strongly preferred the Printed Summary, as they felt it was accessible to all (see Section 8.2.1), unlike approaches relying on access to internet/email.

> *"The web page is okay but when I look at all the participants that we have, there is only one who uses the internet. The rest are old school. They prefer face-to-face or written." BMRNI04 – Research Nurse, medium site*

9.3.2 Health factors

Factors related to participants' health, and their experience while taking part in the trial, may also affect satisfaction with how results are communicated.

We did not collect quantitative data on participants' health (e.g. whether their cancer had progressed, or side-effects they experienced during trial treatment), so are not able to carry out quantitative sub-group analysis on this. However, we do have data on which ICON8 arm they were randomised to, so are able to look for any subgroup effects of this on the efficacy of the Show RESPECT interventions. This is included as an individual-level rather than trial-level factor, as participants are randomised to different groups within a Phase III trial, whereas trial-level factors are those that apply to all participants.

9.3.2.1 Randomised arm

More than 70% of patients in each of the ICON8 arms were quite or very satisfied with how the results of the trial were shared. I found no good evidence that the effect of the Show RESPECT interventions varied by the ICON8 arm women were on (Table 9.2 and Figure 9.2), with the interaction tests for the Enhanced Webpage vs Basic Webpage, Printed Summary vs No Printed Summary, and Email List Invitation vs No Invitation being p=0.424, p=0.543 and p=0.557 respectively. In the qualitative interviews women in both the control and weekly chemotherapy arms talked about being glad of or not regretting how they were randomised. See Sections 7.6.2.2 and 9.2.3 and for more discussion on this.

9.3.2.2 Health at the time results are shared

From the qualitative interviews, patients' own health at the time they receive the results does not seem to have had an impact on satisfaction with how the results were shared. Both patients whose disease had progressed, and those who were in good health, reported being satisfied or dissatisfied. Even the person whose disease had got worse much sooner than average for the trial was not upset about the overall results. Another patient whose disease had progressed felt the results were of limited interest, because they were no longer relevant to her.

However, there was some suggestion from a few patients that they thought that it may influence how other patients prefer to receive results. One patient talked about email being fine for patients who were doing well, but perhaps being less appropriate for patients whose health was less good, or who had less access to support.

> *CLI01: "It would have been fine for me but it may not have been fine for other people. Not everybody has survived this as well as I have."*
>
> *IV So your health status makes a difference to receiving this information?*
>
> *CLI01: "Yes. So, yes, I could receive that by email without a problem. Somebody else might have found that more difficult" CLI01: Patient, large site*

This desire for different modes of communication to those in the arm that did less well overall (as discussed in Section 9.2.3) seemed particularly important if the patient had experienced disease progression.

> *"I think I would have liked the doctors to talk to me about that. If there really was a finding that actually, people were living longer and I'd got secondaries or something, yes, I would have liked to have been spoken to about that rather than finding out on the website." CLI01: Patient, large site*

Site staff also felt that more care was needed when sharing results with participants who were in poor health at the time results are available to share. Understanding of what was happening in terms of patients' treatment was important for sharing results. This led most site staff I interviewed to the view that the results need to come from sites, who have access to this information, rather than trial Sponsors or other organisations who may not be aware of this.

> *"I think you'd probably have to be a bit more careful in terms of sharing results with patients who were very unwell and closer to their end of life. Particularly if they've reached the point where they are, I suppose, have come to terms with the terminal nature of their illness. Sharing information that might bring back difficult memories at that point, might be more difficult. I think it's probably still best practice that if we do have that information available and we're seeing the patient, that we ask them whether they want to know about the outcome of the trial." HLCLI02: Clinician, large site*

> *"I think someone in my role who has access to their clinical records and knows where they are in their treatment plan and has access to their clinical letters, the clinic letters, is always the best person to do it." CLTCI04: Trial coordinator, large site*

9.3.2.3 Experience of side-effects during the trial

From the qualitative data, there did not seem to be a relationship between the severity of side-effects patients experienced during their trial treatment, and their satisfaction with how the results were shared. Those with side-effects seemed to find it comforting to know others had had similar problems.

In the interviews, patients often underplayed the seriousness of the side-effects they experienced during the ICON8 trial. Often they would tell me they did not really have bad side effects, then, later in the interview, they would go on to describe side-effects that would be categorised as serious, for example requiring admission to hospital. This downplaying of side-effects may be because they were expecting to experience even worse side-effects, based on what they expected, or what they had observed in others, or wanting to stay positive.

> *"I didn't really have major side effects. Having said that my bowel leaked, that was pretty much awful, blood clots in my lung, multiple blood clots in*

my lung. And the pins and needles were just awful. And my toes are still really bad, my feet there's still pins and needles but my fingers are all fine now. That was a major side effect, the pins and needles. And as far as the, yes, the debilitating side of chemotherapy I was quite lucky I didn't allow it or it didn't pull me down as much as I have seen other people." BLI01: Patient, large site

9.3.3 Other individual-level contextual factors

There are many other contextual factors that may influence satisfaction with how trial results shared. The ones discussed in this section are the ones that came out as potentially important in my qualitative analysis. Other individual factors that influences satisfaction, that have been discussed elsewhere in this thesis are patients' desire to receive (or not receive) the results (Section 7.4), and the level of information they would like (Sections 8.3.1 and 8.3.5).

9.3.3.1 Relationship between site staff and participants

Participants had been taking part ICON8 for between five to eight years, with face-to-face follow-up visits initially every 6 weeks straight after treatment, reducing to 3 monthly after 9 months, then 6 monthly after two years. During this time, some patients had developed a very close relationship with their site staff, particularly research nurses. This was especially the case at small and medium sites where the research nurse had been the same throughout the course of the patient's trial experience. Having a good relationship with their research nurse or oncologist meant that patients felt able to ask questions about the results, if needed.

"I suppose to some extent, it's on the research nurses because the two that I saw are really great. I get on really well with them and I don't feel afraid to ask them any questions. But I think that's more a personal thing really. It's quite difficult for somebody if they can't relate to the people they're seeing, for whatever reason, obviously the next best option would be to have some paper to take away and read in their own time." DMI01: Patient, medium site, close relationship to site staff

However, some patients did not want to bother busy site staff with questions (at least until they were scheduled to see them for a routine check-up), so had less opportunity to ask questions or seek clarification, and may have forgotten their questions by the time their scheduled visit arrived. In that situation, having alternative routes to access support or ask questions (such as the FAQ section and links to support on the enhanced webpage/email) might be particularly useful.

"I do have numbers to ring the nurses at the [BL Hospital], but you never really want to bother them." BLI01: Patient, large site

"I think by the time they had it in the post and they came back to clinic, they'd forgotten all about it really and that's probably why they didn't

speak to the PI [Principal Investigator]." AMRNI05: Research Nurse, medium site

Patients' relationship with site staff seemed to affect satisfaction with how results were communicated; some questionnaire respondents explicitly cited it as a reason for their satisfaction. Nearly all the patients I interviewed who said they had a close relationship with their site staff were satisfied with how the results were shared.

"My oncologist and research nurse have been excellent and I respect their dissemination of information, as it is on a personal level" FSQI02: Patient, small site

Some patients with a close relationship with site staff would have preferred to receive directly from them, rather than via a Printed Summary or webpage, but were still satisfied with the way the received results, and recognised that this personal approach may not be the best for patients without that close relationship.

"I think they should do them face to face really. I don't know if that's… I mean, the thing is, you build up a relationship with your trial nurses because we see them quite regularly or every time we go for a hospital appointment. So, I think it would be really nice if they presented that themselves, obviously backed up with information. I think because you're feeling vulnerable anyway and I think if you've already built up a relationship with people, then it's easier to talk to them." DMI01: patient, medium site, close relationship with site staff

"I don't know, because we are a smaller centre and our numbers don't tend to be like a big teaching hospital, we have that more personal approach, so we know our patients very well, we know the families very well, so it makes it easier for us in that respect. I'm not saying, if it was a teaching hospital you could follow the same principles, but here, we generally have that closeness." CSRNI01: Research nurse, small site

The number of trial participants at a site seemed to influence site staff's views on how results should be shared. This is linked to feasibility issues, with posting information or talking to participants being less practical if they have large number of participants, but also related to how well staff knew participants. Some staff at large sites, in particular those who had worked on ICON8 for less time, felt uncomfortable contacting patients (e.g. by telephone) as they did not know them, were not sure what their current situation was, or whether they would want to be contacted. The two site staff members who felt this would have preferred an opt-in approach, as they did not know whether their patients would want to know the results, and the work involved was time-consuming. They were also worried about reminding participants that they had cancer.

"I guess this is quite easy for me to say though because we don't have an awful lot of patients on the ICON8 trial, so this is not labour intensive for

me and [research nurse]. It will just require me to initially send out some things, a bit like what we've done already basically, and she'll follow it up with a follow-up call. It's not really that much of a problem. If we had, like, 50 or 60 patients on this trial, that could be an issue, couldn't it?" GMTCI02: Trial coordinator, medium site

Patients I interviewed who did not have a close relationship with site staff were less satisfied with how the results were shared. For some patients this was because they struggled to understand the results, or access them, and not having a close relationship with staff meant they did not want to contact their research nurse for clarification or to ask for the information by post. In one case the dissatisfaction was around the results summary not being detailed enough, and being perceived to be received long after the results were known.

9.3.3.2 Patients' understanding of the trial and equipoise

In the qualitative interviews it became clear that not all participants had fully understood the concept of randomisation at the time they joined the trial, or were not in equipoise, having clear preferences for which arm they wanted to be in. Those patients whose understanding of the purpose of randomisation was less good, or who had strong views about which group they wanted to be in, tended to be less satisfied with how the results were shared.

"I'd be miffed if I was a person on three-week, on the control group. In fact, probably I would have pulled out and I know that sounds selfish but I would have been so annoyed about not being able to have it weekly." DLI01: Patient, large site, randomised to weekly chemotherapy

9.3.3.3 Patients' expectations around receiving results

There was no clear pattern as to satisfaction with how the results were shared based on whether patients were expecting to receive the results or not. Some participants had been told at the point of joining the trial that they would receive results, whereas others did not expect to receive them (or even be alive when the results were available).

"It's amazing because as I said earlier, I wasn't expecting to even get any results let alone all this. So anything was going to be wow to me, wasn't it?" BMI01: Patient, medium site

9.3.3.4 Patients' access to support

The patients I interviewed varied in terms of how much support they had access to, from family and friends they could talk to about their health, and patient support groups. Some patients and site staff felt that the links to further information and support and FAQ features of the Enhanced Webpage and Email List may be particularly valuable for patients with less access to support, or who feel less able to ask their site staff questions.

"The only real feedback I had was from some of the written in [E Hospital] with that patients just were a little bit shocked it wasn't better prognosis all around. Just not having anyone to turn to at the time when it landed on her letterbox because she lived alone. So, all those patient factors are really important whether they've got someone with them when they're going through. Just like opening exam results, you initially need someone with you." EBLMCLI02: Clinician, large and medium sites

9.4 Discussion

9.4.1 Summary of key findings

The condition being studied in a trial, what the results show, and length and type of follow-up have implications for how results are shared. Trials in more serious conditions, or with more complex or potentially upsetting results (e.g. when one arm did less well than others) may need to offer participants additional support, for example through sharing results face-to-face, or offering follow-up appointments or phone calls with clinicians or research nurses if results are shared via written summaries. Trials with long follow-up, where patients may build close relationships with site staff, need to provide a way for the results communication to be personalised to some extent, to reflect this relationship. This may be through staff members adding personalised cover letters or compliments slips to Printed Summaries or Patient Update Information Sheets, or through phoning the participants before and/or after the results are posted out. This may be less important where relationships are less close (for example, if the site has had considerable turnover of staff over the course of the trial, or in trials where follow-up is shorter or not done through site staff).

Participants' age, educational qualifications, randomised arm of the ICON8 trial, and frequency of use of internet or email seemed to have had little impact on the effect of the Show RESPECT interventions on satisfaction with how the results were shared. These quantitative findings conflict with qualitative findings, where interviewees suggested that older and less frequent internet/email users would be less satisfied with webpages or email as approaches to sharing results, compared to Posted Printed Summaries. Less computer-literate patients often had coping strategies (such as enlisting the help of families and friends to access results) which helped them access results, and those I interviewed did not seem to mind having to get this help, which may explain why we did not observe a difference in satisfaction, nor reporting that it was easy to access results in the quantitative data.

Health-related factors did not seem to have a major impact on how participants reacted to receiving the results, with women from all ICON8 arms able to find positives from how they had been randomised, perhaps in order to reduce

distress or regret. There were not obvious differences in reaction between those whose disease had progressed, and those whose disease had not progressed by the time they received results. Those who had experienced serious side-effects found it interesting to read about the side-effect results and put their own experience in context. Patients I interviewed who had less understanding of the trial, equipoise and the purpose of randomisation, tended to be less satisfied, reinforcing the importance of informed consent, and the need for results summaries to include reminders of some of these key concepts.

9.4.2 Strengths of this study

The main strength of this study is the triangulation of qualitative and quantitative data from patients and site staff. The qualitative data allow us to explore the reasons behind the quantitative results. This is especially valuable for surprising results, such as the Posted Printed Summary not being superior to No Posted Printed Summary in terms of being easy to access. Having qualitative data from site staff, who generally work on many different trials with different populations and results scenarios, allows us to explore their views on the extent to which the results we saw within Show RESPECT are influenced by trial-level factors, as they can compare their experience within ICON8 with any previous experience of sharing results in other trials.

9.4.3 Limitations of this study

This chapter is only a partial exploration of the other factors that influence participant satisfaction with how trial results are shared with them. The quantitative data are limited as I was only able to collect data on a few potential factors: age; highest educational qualification; frequency of internet/email use and ICON8 arm. Data on ethnicity or socio-economic status was not available in the ICON8 dataset, and the Show RESPECT study steering group decided not to add questions on this topic to the patient questionnaire as it was felt this might put some patients off completing it. I am therefore unable to look at how these factors influence satisfaction with how results were shared. I did not directly measure literacy or health literacy, using highest educational qualification as a proxy measure, as measuring health literacy is complex[115], and adding questions to assess literacy or health literacy within the questionnaire risked reducing our response rate. Similarly, I did not directly assess computer literacy, using frequency of internet/email use as a proxy measure, as this was simpler to assess within a paper questionnaire, and captures challenges of accessing the internet/email (e.g. lack of internet connection at home) rather than just the skills needed if relevant technology is available.

Show RESPECT was powered based on the primary outcome in the overall patient respondent population, and not for the sub-group analyses. The sub-groups were pre-specified, but I cannot rule out there being a real sub-group effect that we were unable to detect due to lack of power. I had so few respondents who said that English was not their first language that I was unable to carry out subgroup analysis on that factor, and cannot draw any conclusions as to how the Show RESPECT results would apply to those receiving results in a second language. For some of the factors discussed in this chapter, such as health at the time results were shared, experience of side-effects, access to support, and understanding of the trial, only qualitative data are available, but given the complexity of some of these factors, they may perhaps be better explored qualitatively anyway.

Show RESPECT took place within the context of a single trial, meaning care is needed when transferring the results to different patient populations or results scenarios. In order to understand the extent to which the results reported in Chapter 5 were influenced by trial-level factors, we have to rely on patients and site staff views on hypothetical scenarios (e.g. if the trial had been in a less serious disease, or had found a clear benefit), rather than comparing data from patients who have actually received results in these different scenarios.

9.4.4 Conclusions

When deciding how to communicate trial results, trialists need to consider the characteristics of the patient population of that trial, and also trial-level factors such as the seriousness of the condition being studied; what the trial results show; and the closeness of relationships developed between site staff and patients over the course of the trial. Trials that find clear differences between the arms may need to communicate results to people in the group that did less well overall in a more personal way, or offer further support to these people. Where relationships between site staff and patients are close, allowing some degree of personalisation of results communication may be important. Posted Printed Summaries seemed to benefit all patients, not just the 4 in 10 who used email or internet less than daily, suggesting the results may be transferable to patient populations with higher proportions of frequent computer-users.

10. Discussion

10.1 Overview of scope of this chapter

Through Show RESPECT, I sought to

1. Evaluate the effectiveness of the Enhanced Webpage, Posted Printed Summary and Email List on participant satisfaction, understanding, providing the information patients wanted to know, and ease of finding out the results (Chapter 5)
2. Evaluate the acceptability and feasibility of the interventions and process used within the Show RESPECT study from the site staff perspective, including the resources required to implement the interventions at site and CTU level (Chapter 6)
3. Describe the experience of patients (Chapter 7) and site staff (Chapter 6) around receiving/sharing the ICON8 results, within the broader setting of their involvement in the trial, their previous experience and wider context
4. Explore the aspects of the mode of communication that affected satisfaction with how the results were shared, from both patient and site staff perspectives (Chapter 8)
5. Explore the other factors that influenced satisfaction with how the results were shared, from both patient and site staff perspectives (Chapter 9)

This chapter brings together the key results from my research, discusses their strengths and weaknesses, and puts them in the context of the wider literature. It then sets out areas for further research. I then present a framework of factors to be considered when deciding how to communicate the future trial results to participants, linked to my findings. I go on to make some overarching recommendations for trialists, site staff, funders and ethics committees, to help make sure the trials community does a better job of fulfilling our ethical obligation to offer results to participants in the future. This is followed by a brief conclusion, ending with comments from the Patient Representative on the Show RESPECT study steering group.

10.2 Summary of key findings

10.2.1 Patients' perspectives on the effectiveness of the Show RESPECT interventions

Nine in ten women taking part in the ICON8 trial of ovarian cancer treatments wanted to be told the results of the trial they had taken part in. Patients at sites which were randomised to the Printed Summary (in addition to a webpage)

were more likely to be satisfied with how the results were shared and were more likely to find out the results than those at hospitals randomised to no Printed Summary. Generally, patients who received the results through any of the Show RESPECT interventions said that the information was easy to understand and find. While most participants said the information told them everything they wanted to know, the proportion of patients saying this was higher among those randomised to the Enhanced Webpage rather than the Basic Webpage. ICON8 participants said they were likely to take part in future research and recommend it to others. These findings suggest that trials with similar participant populations to the ICON8 ovarian cancer trial (mainly women aged fifty or older) should use Printed Summaries alongside an Enhanced Webpage. This will enable more people who want to know the results to find them out, improve satisfaction, and give people all the information they want to know.

10.2.2 Sharing results with trial participants: the perspective of site staff

Site staff were strongly supportive of sharing results with participants, with benefits including showing that participants' contribution to trials are respected and valued, repaying trust, giving something back to participants, increasing awareness of the importance of research, and helping participants process their trial experience. They felt that the process of sharing results with participants in Show RESPECT was generally straight-forward and not too time-consuming, although the time required was more of a challenge for some staff at sites with large numbers of participants. The approaches adopted in Show RESPECT (Patient Update Information Sheet with links to Basic and Enhanced Webpages and Email List; Posted Printed Summary) were feasible for staff at the participating NHS hospitals to implement, and acceptable to those staff, and could potentially be adopted by other studies in similar settings. Trials with sites that have very large numbers of participants will need to consider how to support these sites with sharing results with participants.

Sharing results via a Patient Update Information Sheet followed by an opt-out Posted Printed Summary increased costs per participant to sites by around £14 compared to a Patient Update Information Sheet with a link to a webpage ± Email List sign-up link alone. Most of these costs were staff time. The Email List intervention was the most time-consuming for clinical trials unit staff, which accounted for a third of the hours spent on developing, reviewing and disseminating the Show RESPECT interventions. The time and costs of sharing results with participants are small in comparison with the overall costs of trials, which often run into millions of pounds, and time required for other trial processes.

10.2.3 Patients' thoughts and feelings on receiving trial results

Patients join trials for potential personal benefits and to help other people. Nearly all participants wanted to know the results of the ICON8 trial, to help them understand whether their aims for taking part were achieved, and to gain closure. The large majority of patients were glad to find out the results of the ICON8 trial, describing them as interesting and important, despite some being disappointed that weekly chemotherapy did not improve outcomes. The large majority of those who reported finding the results upsetting did not regret finding out the results. Participants should be offered the results of trials even when those results may be disappointing or upsetting.

Offering trial results to the families of participants who die during a trial may have value for the bereaved, but needs to be done sensitively to avoid causing unnecessary distress. Further research is needed to explore how to share results with bereaved families of trial participants.

10.2.4 What aspects of the Show RESPECT interventions influenced participant satisfaction?

Printed Summaries sent by post were seen as accessible to all, especially those with limited computer literacy or access to the internet, and made it easy for patients to keep information for future reference. The information contained in the results summaries tested in Show RESPECT covered the topics most participants were interested in, and was written in an understandable way. The extra features contained in the Enhanced Webpage (the short video, links to further information and support, and option to send in questions to be answered on the webpage) may be useful for some patients, even if not accessible to all. Some personalisation of the Patient Update Information Sheet (and Posted Printed Summary), such as including a personal covering letter or compliments slip, was felt to be important by some patients and site staff. Opt-out approaches to sharing results may be better at ensuring patients who want to find out the results receive them, but the option to opt-out needs to be made clear. For trial populations like those in ICON8 (mainly women in their 60s or older), Posted Printed Summaries have several advantages, including accessibility, and being easy to file results for future reference, or show to others.

10.2.5 What other factors influence satisfaction with how the results were shared?

The ICON8 trial did not show a benefit from the research arms of weekly chemotherapy; in some ways this made the results easier to receive for

patients in the control arm, as no-one had missed out on a superior treatment. Trials that find clear differences between the groups may need to communicate results to people in the group that did less well overall in a more personal way, and/or offer further support to these people.

Communication of results takes place within the context of relationships that have developed over the course of the trial between patients and site staff. In the case of some patients and site staff, these relationships were close, creating a need for how the results were shared to reflect this, for example through some degree of personalisation.

The Posted Printed Summary increased satisfaction with how results were shared across all ages and levels of education and computer use, indicating that the overall results (reported in Chapter 5) were not solely due to the patient population in ICON8 being older and less comfortable using computers. This suggests the findings may be transferable to patient populations with higher proportions of frequent computer-users.

10.3 Strengths of this study

This randomised controlled trial contributes to the scant evidence base on how to communicate study results to trial participants, providing high quality evidence to a field that is dominated by observational data, surveys asking about hypothetical scenarios, and expert opinion. Show RESPECT is the first randomised controlled trial to compare different communication modes for sharing results with trial participants. The randomised design reduces the risk of the results I observed being due to differences between the groups other than the allocated interventions. Show RESPECT is embedded within a clinical trial, where I gathered data from participants and site staff on their actual experience of receiving or sharing results, unlike much of the published literature on the topic, where survey studies tend to focus on hypothetical scenarios, ("how would you like to receive/share results?", rather than "did you like receiving/sharing results in this way?") necessitated by the rarity of trials sharing results with participants[22, 39, 41, 45, 116].

The mixed methods approach, using both quantitative and qualitative data collection and analysis, allowed me to explore not just quantitative associations, but also the reasons behind those associations. Collecting data from site staff as well as patients is another strength, as, for trials like ICON8, site staff are key actors in the process of sharing results, without whose support the interventions would not work. Triangulation of the different data types and sources using the 'Following a thread' approach[96] allowed me to create a multi-faceted picture of the topics discussed, without having to reduce

qualitative data to frequency counts in order to integrate different data sets, as required by other approaches such as the triangulation protocol[97].

The interventions tested within Show RESPECT were designed to be easily replicable in other trials which do not have access to extensive communications support or resources. This increases the transferability of our findings. The ICON8 trial context in which Show RESPECT took place is typical of cancer treatment trials run by the MRC Clinical Trials Unit at UCL and many other CTUs around the UK, in terms of range of site characteristics, and the lack of direct interaction between the participants and trial Sponsor. This also increases the transferability of my findings.

The qualitative data I collected provides a rich understanding of the perspectives of patients and site staff on the experience of receiving or sharing trial results. I applied an established theoretical model (the Information Seeking and Communication Model[105, 106], described in Section 3.9.1) increasing my 'information power'[100] and allowing me to ground my conclusions in the context of existing knowledge about the process of information seeking and communication.

10.4 Limitations of this study

The main limitation of Show RESPECT is that it was carried out within the context of a single trial, raising questions about the transferability of the findings to trials with different patient populations, diseases, results scenarios and settings. My patient population was women with an average age of 67, nearly all of whom had English as their first language, and who were ovarian cancer patients at NHS hospitals in England and Wales, and the results we communicated showed no evidence of a difference between the treatment arms. I have no data on the ethnicity of respondents, nor on factors such as socio-economic background, so am unable to explore how these factors influence satisfaction with the different communication approaches tested in Show RESPECT. I may have seen different results if we had carried out the study in the context of a different trial. For example, a trial looking at treatment for testicular cancer with a young male patient population may have different results in terms of desire to find out the results (given the better prognosis in testicular cancer, it is conceivable that a higher proportion would not be interested in the results as they 'move on' from their illness). They may also prefer to find out the results via online approaches, as they may be more comfortable with this than the ovarian cancer population are. Trials carried out in settings or populations which have less access to the internet than ICON8 may find even larger benefits from Printed Summaries.

Another limitation of this study is that not all ICON8 sites took part in it. It could be that sites that took part in Show RESPECT were systematically different to those that did not, for example with staff being more committed to or able to share results with participants, meaning the excellent results we saw in terms of distribution of the Patient Update Information Sheet and Printed Summary may not be replicable in all sites. Our study does demonstrate that, where there is sufficient will, results can be shared with participants by sites of all sizes, and that there is desire on the part of participants to receive these results.

The factorial design means that I have no data on the effectiveness of sharing results using a Posted Printed Summary without also providing a link to a webpage. This means I am unable to say how effective a Posted Printed Summary without a link to a webpage ± an invitation to join an email list would be. However, setting up and providing a link to a Basic or Enhanced Webpage in the Patient Update Information Sheet requires relatively little extra time and cost (Section 6.6.3), so it may be worth offering both a webpage and Printed Summary anyway, giving patients a choice of how to receive the results.

My study focuses solely on the communication of overall trial results, rather than individual results. It took place within an open-label trial, where participants were aware of their own outcomes (e.g. disease progression). Placebo-controlled trials may raise additional issues to consider, as may trials where participants are unaware of their individual results[7].

10.5 Results in context

10.5.1 Results in the context of what is known about approaches to communicating results to participants

My results provide the first randomised evidence comparing different approaches to sharing results with participants, showing that Posted Printed Summaries in addition to webpages improves patient satisfaction with how the results are shared, compared to webpages alone. Previous observational research has shown that sending information by post is highly acceptable, or preferred by participants[13-15, 19, 20, 37, 42, 43, 45-47, 117, 118]. My finding that different approaches (e.g. face-to-face communication), or more support, may be necessary to communicate complex results, or results that could be perceived as bad news by some participants, supports recommendations put forward by research ethicists[119].

Data from the UK Office for National Statistics in 2019 shows that 10% of the UK population are classed as internet non-users, having either never used the internet, or not used it in the last three months[107]. Internet non-users

are more likely to be women, over the age of 65, disabled, or economically inactive (particularly those on long-term sick leave)[107]. Households with lower incomes are also less likely to have an internet connection[107]. While the number of internet non-users has been declining in recent years, trials should be careful about relying on the internet or email to share results with participants, particularly if their trial population overlaps with some of the groups most likely to be internet non-users. Failure to take this into account could exclude a significant proportion of participants from accessing results. Other ways of receiving trial results must be offered to participants.

I found no evidence of a difference in reported ease of finding the results between the Posted Printed Summary and No Posted Printed Summary groups in my quantitative data. This is surprising, given that four in ten respondents reported using the internet or email less than daily, with 15% never using them, so may be expected to find it easier to receive results by post rather than having to go online to find them. In the interviews some participants randomised to No Posted Printed Summary did report difficulties accessing the webpage or email list. These challenges were generally overcome through the help of family members. Patient and site staff interviewees generally felt that Posted Printed Summaries were likely to be more accessible than webpages, particularly for those with limited access to the internet or computer literacy. It may be that as so many things now rely on access to the internet, participants who struggle in this area are used to having to get help from relatives.

10.5.2 Results in the context of what is known about trial participants' desire to receive trial results

Nearly all patients in the Show RESPECT study wanted to be informed of the results of ICON8. This is consistent with findings from previous studies[14, 15, 18, 43, 120], which have suggested that not finding out the trial results may increase the burden associated with trial participation that participants experience[121]. Participants' desire to find out trial results seemed to link back to their motivations for joining the trial: the potential for it to benefit themselves, and/or future patients. These motivations for joining the trial are consistent with previous studies, including a qualitative study in diabetes trial participants[122] and an overview of systematic reviews that looked at why patients take part in research, where personal benefit and altruism were two of the three main reasons[123]. The issue of trust, which was the third main reason found in the latter study, was not prominent in my data.

Patients liked being given the choice over whether to receive results, and 7% of patients did not wish to receive the results. This reinforces recommendations that a two-stage approach should be used, offering results and then providing

them, rather than simply distributing results to everyone[124]. Choosing not to access results was, for some patients, a way of protecting themselves from potentially finding out that they missed out on the best treatment. This concept of people choosing what information to engage with or not as a protective mechanism is similar to findings from the BRACELET study, where some bereaved parents of babies who died in a neonatal trials chose to throw away communication from the trial if they felt it might be upsetting for themselves or their partner[55].

10.5.3 Results in the context of what is known about how participants react to receiving results

Fear of upsetting participants has been reported as a barrier to sharing results by some trial staff in previous studies[34, 35, 39]. In Show RESPECT, 16% of patients reported finding the results upsetting, which is similar to levels of upset reported in previous studies[37, 43]. However, my results provide reassurance that, even though some participants do find the results upsetting, nearly all still do not regret finding out the results, supporting qualitative findings from the BRACELET study around sharing trial results with parents of babies who died during a trial[47]. Show RESPECT participants' positive reaction to receiving trial results is also consistent with that reported by previous studies[17, 37, 43, 44, 46].

Nine in ten of Show RESPECT participants said they would be likely to take part in future research, and recommend it to others. This is similar to the findings of previous surveys of trial participants[19, 20, 125]. This is impressive in a trial in which many women experienced unpleasant side-effects from the trial interventions and control, and the trial overall did not find a benefit from the interventions. Given the results of ICON8, patients' positive attitude to research is likely to be down to other aspects of their trial experience, including the quality of care they received, increased monitoring compared to non-trial treatment, the close relationships that developed between many patients and their site staff, and a feeling of having contributed to something worthwhile, even if it did not lead to an immediate change in clinical practice.

10.5.4 Results in the context of what is known about what information should be included in results summaries for participants

In Show RESPECT, patients were most interested in knowing the main efficacy results, their implications for participants and future patients, and information on side-effects. This is similar to findings from a qualitative study of participants in two surgical trials, which found that implications for the future, and the overall success of the trial, were important[117]. The RECAP study

found that Sponsor Details, Trial Identifier and full title were considered among the least important information items for inclusion in a participant summary[60], which supports my finding that participants found this information hard to understand and unnecessary (Section 8.3.4). Both RECAP and the study within surgical trials found that a 'thank you' was among the information items considered least important, however I found that, for the Basic Webpage (which did not have a thank you), interviewees noticed it was missing, and commented that it made it feel less aimed at participants, and less personal, contributing to this webpage being less preferred than the Enhanced Webpage. The difference between these two other studies and Show RESPECT may be because in those studies participants were asked to comment on information items in principle, rather than within the context of an actual results summary for a trial they had contributed to. I have been unable to find reports of other qualitative studies that have looked at participants' views on the contents of results summaries for the trial they have taken part in, suggesting that Show RESPECT may be the first study to look at this.

10.5.5 Results in the context of what is known about how well patients understand trial results

Previous studies of health literacy in the UK have shown high levels of health illiteracy[126, 127], with low levels of health literacy and functional health literacy being particularly common in older patients[126]. It is therefore pleasing that 80% of Show RESPECT respondents agreed that information was easy to understand, with no significant differences by education level. Interviewees were able to give accurate summaries of the results during the qualitative interviewees. The proportion reporting the results were easy to understand is substantially higher than that reported in a study within the context of a breast cancer trial, where only 56% said the results letter was easy to understand[19], and a survey of cancer trial participants, which found less than half reported fully understanding the results[16]. This difference is likely due to the work put into developing the summaries, using principles of Plain English, and input from patient representatives at several stages of developing the text. The results letter used in the breast cancer study had a Flesch Kincaid Grade Level[128] of 13.1[19] (indicating approximately 13 years of education would be required to understand it), which is substantially higher than the Flesch-Kincaid Grade Level of our summary, which was 9.7. It is not unusual for 'plain language' summaries of study results to be hard to read, with many demanding much more advanced reading skills than most people possess[129]. A study linked to a trial of antibiotics for suspected pre-term labour developed a leaflet with extensive input from patients, and saw similar levels of comprehension to

our study (86%)[37], suggesting that involving patients in developing results summaries may be a helpful strategy for improving comprehensibility.

10.5.6 Results in the context of what is known about site staff views on sharing results with participants

My finding that site staff are strongly supportive of the principle of sharing results with trial participants is consistent with the results of previous surveys of trial staff[18, 22, 28]. Site staff I interviewed talked about participants being entitled to know trial results, which chimes with findings from a study looking at communication of results in two US trials run by Pfizer, where site staff talked about participants having the right to be informed of trial results[42]. Concern about the emotional impact on patients of receiving trial results was raised by some of my site staff interviewees, and has been reported as a barrier in other studies[22, 39]. The importance of discussing how results will be shared during the Informed Consent process has also been reported in previous studies[39].

10.5.7 Results in the context of what is known about the resources required for sharing results with trial participants

I found that the process used to share results within Show RESPECT, via Posted Printed Summaries, was feasible for site staff to implement. This echoes findings from previous research carried out by the Center for Information and Study on Clinical Research Participation (CISCRP), where study staff reported disseminating trial results summaries was simple, straightforward and not time-consuming, and that queries from patients were rare and did not require substantial amounts of time to deal with[42]. The estimated time required from study personnel to send out the lay summaries is similar between Show RESPECT and that study, although some Show RESPECT sites did take up to 7 hours sending out the summaries. It is unclear from the CISCRP study how many participants were at each site, so the difference in time may be due to some ICON8 sites having considerably larger numbers of participants.

Costs are frequently cited as a barrier to sharing results with participants[9, 18, 35]. My study is the first to provide detailed information about the costs of sharing results with participants through different approaches, from both a site and CTU perspective. One study has published information on the costs of an online meeting for participants and other stakeholders, which cost £1624[130]. As 89 people attended the meeting this works out at £18.25 per attendee. However, the estimate does not include the 40 hours of staff time required to organise the event, would considerably increase the costs. Only 12% of trial participants attended the meeting, and it is unclear whether those who wanted

to know the results but did not attend have been able to find out the results in other ways. Another study provides the costs of carrying out PPI to develop a results summary, and print and post it, alongside the costs of a research assistant to coordinate the study. Excluding the costs of data collection to evaluate the intervention, these costs come to €7,681.91, or €76.06 per participant the results were shared with[119]. The other cost estimate reported in the literature is from a study which sent out leaflets by post, with printing and postage coming to £1.22 per participant (similar to my estimates for printing and postage), but not including the staff time required to develop or do the mailing[15].

The average cost per participant of sharing results that I report in Chapter 6 are small in relation to the overall costs of phase III clinical trials. If results had been offered to all eligible ICON8 participants in Show RESPECT via a Patient Update Information Sheet, Posted Printed Summary and Enhanced Webpage, costs to the clinical trials unit and sites would come to around £40 per participant in total. This is around 0.5% to 1.4% of the average UK trial cost-per-participant, using cost estimates of £2987 or €9758[131].

10.5.8 Results in the context of the Information Seeking and Communication Model

The Information Seeking and Communication Model was helpful for my analysis as it describes the process and factors that influence process from both information providers and information users' perspectives. Many models of the communication process focus solely on one perspective[132]; or focus on communication to change behaviour/practice[133-136], rather than to inform, as was the case with the ICON8 results. The Information Seeking and Communication Model was developed based on a review of existing models from the field of Library Information Science and communication studies, and incorporates many of the insights from these models[105]. It has been used empirically in research into healthcare communication, both by the original authors[106] and others[137-139]. Using the Information Seeking and Communications Model means that the terminology I use in my results can easily be related to other research in the field, providing clarity and allowing comparisons to be made. Identifying it as useful part way through my analysis (after an extensive search, and review of more than 50 potentially relevant theoretical frameworks), rather than from the start, means I am confident that I was open to the possibility of other concepts being identified in the data (i.e. my coding and theme development was inductive as well as deductive).

Although the model fits most of my data well, one concept that I identified was not explicitly covered by ISCM diagram was 'Information', (what the

information being communicated actually is, and how that affects how the information is communicated and received). This includes the specific information items included or excluded within the information products, the framing of that information, the language used and the level of information provided. Data on participants' views on sharing results with others, including family members, is beyond the scope of the Information Seeking and Communication Model. Conversely, not all concepts from the Information Seeking and Communication Model were evident in my data; for example the 'Act/decide' concept was not relevant for this particular data set, as the information being communicated was communicated to inform rather than persuade, and the information did not have direct relevance to these specific patients' future treatment.

Therefore, I propose revisions to the model shown in Figure 3.3 to explicitly incorporate 'Information', including its content, framing, the language used and level of information. It may also be helpful to separate out out-takes from outcomes (in line with the terminology used by the Association for Measurement and Evaluation of Communication Integrated Evaluation Framework[140]), to recognise that not all information sharing is seeking to inform decisions or lead to actions, and may be primarily aiming just to share knowledge. I propose adding 'thoughts' and 'feelings' to the 'Assess, use or ignore communication' box, as from my data these were both part of how patients assessed or chose to use or ignore communication. These revisions to the Information Seeking and Communication Model may be helpful for others studying the different sorts of impact communication may have, and those interested in exploring how the information being communicated affects the process and medium for communicating it, and the effect that has on how it is received, used or ignored.

10.6 Areas for further research

Further research is needed to assess interventions like those tested in Show RESPECT in different trial populations, settings, disease areas, trial designs or for trials with different results scenarios.

NHS Digital have recently launched NHS DigiTrials[141]. One of the services DigiTrials is planning to offer is distribution of research results to participants, via post, text messages and email. There is a fee for this service, but, for large trials, it is likely to be less than the costs of sites doing this. This may be particularly appealing to trials where sites have large numbers of participants, as my research found that, while most site staff said the process was feasible and did not take too much time, some staff at sites with large numbers of

participants did find the time required to post out results challenging. However, there may be drawbacks to this approach, as it would take the communication of results out of the context of the relationships developed between site staff and participants, which, as discussed in Section 9.3.3.1, was important for some, and not allow true personalisation (discussed in Section 8.5). Evaluation of this approach is needed to look at its acceptability to patients and site staff, and identify when it is appropriate, and when it would be important for results to come from site staff instead.

Another issue that requires further research is sharing results with the relatives of trial participants who die during a trial (as discussed in Section 7.10.2), to see if this is something that relatives want, and if so, how it can be done sensitively.

10.7 Factors to consider when deciding how to share results with trial participants

Sharing results with trial participants is a surprisingly complex issue. There is unlikely to be a single approach for sharing results with participants that will be appropriate for every trial. My research has focused on a single trial, so care is needed when transferring these results to other settings. However, I have identified several factors that I believe trialists should consider when deciding how to share results with participants. While these cannot be summarised in a simple algorithm, I have developed Table 10.1 to help trial teams think through these issues as part of their planning process.

Table 10.1: Factors to consider when planning how to share results with trial participants

Factor	Notes	Relevant sections
Information Users – Who are your trial participants?		
What are the demographic characteristics of your trial participants?	What is their: age, socio-economic status, education level, health literacy, computer literacy, access to the internet?	9.3.1
How well are your participants likely to be?	How is their health at the time of receiving results? How was their health and experience of side-effects during the trial?	9.3.2
What expectations do your participants have around receiving trial results?	What did you put in your Patient Information Sheet? Do you need to get ethics approval for any changes to how you plan to share results?	7.3, 9.3.3.3

Factor	Notes	Relevant sections
What will participants want to do with the results?	Will participants want to keep results for future reference? Will participants want to share results with others?	7.8.2, 8.2.1, 8.4.3, 7.8.3
Information – What do your trial results show?		
What do your trial results show?	Will it be seen as good / bad / neutral news by some/ all participants?	9.2.3
How complex are your results?	Are your trial results complex (e.g. there is important heterogeneity between sub-groups, or do different outcomes go in different directions)?	9.2.3
Information provider – Who should share the results?		
How close are relationships between site staff and participants likely to be?	How long were participants in the trial for? Was follow-up done face-to-face? Which organisation or individual was their main point of contact for the trial? Does the communication need to be personalised to reflect the relationship between site staff and participants?	9.3.3.1 8.5
How many participants do sites have?	Will sites with large numbers of participants have sufficient resources to share results?	6.5.2
Resources available – What budget, expertise and staff time is available for sharing results?		
What budget do you have for sharing results with participants?	Have you budgeted for costs such as printing and postage?	6.6
What expertise around developing patient-facing communications tools do you have?	Do you have access to expertise on this within the team, through partners or paying for specialist support?	6.6.3
Is this activity seen as a priority for clinical trials unit staff?	Is sharing results with participants incorporated in clinical trials unit Standard Operating Procedures and trial protocols?	6.6.3
Has sharing results been included in agreements with sites?	Do sites know this is a trial activity they are expected to do (if you are planning for the results to be shared by site staff)?	6.6.2
Information product – What tool(s) will you use for sharing results?		
What will participants want to know?	Can participants who want different levels of information find out what they want to?	1.8, 8.3, 10.5.4

Factor	Notes	Relevant sections
What language will your participants understand?	What languages was your Patient Information Sheet available in? Do you know how to write in plain Language? How will you get feedback from PPI contributors about your draft results summaries?	1.9 10.5.5
How will you make your information product attractive and easy to use?	Do you have the skills to do this in-house? Do you have good templates to base it on? Do you have the budget to pay for a designer?	1.9.5 8.4.1 8.4.2.1 8.4.2.2 8.4.3
Can you give participants a choice of information products?	Is it feasible for you to provide more than one way for participants to access the results?	8.2.5
Process – How you will prepare and support participants receiving results?		
How will you prepare participants for receiving results?	What did your Patient Information Sheet say about how and when results will be shared? How will you inform participants the results are available?	6.5.1.1
Will you use an opt-in or opt-out approach?	How and when will you give participants the choice of whether to receive results? Are most of your participants likely to want to know the results (if so, an opt-out approach may be best)?	7.4, 8.6, 10.5.2 5.2.5
How will you provide support to patients who have additional questions or are distressed by the results?	Are participants still in follow-up? Can they still access support from their research nurse/study clinician? What other support is available to them to help understand the results, or deal with them emotionally?	9.3.3.4 8.3.9
Communication medium – How will the information product reach participants?		
Which communication mediums are likely to be accessible to your participants?	How can you make sure the results are accessible to all your participants?	5.2.8.2 10.5.1
Where will participants receive results?	Will participants prefer to receive results at the clinic, where support may be immediately available, or in the privacy of their own homes, where they can process it in their own time?	8.2.1
Timing – When should results be shared with participants?		

Factor	Notes	Relevant sections
How urgently do results need to be shared?	Are your results likely to receive media coverage? If so, how can you make sure participants do not first find out results via the media? Do your results have implications for the future treatment of your participants? Are participants still in follow-up? If so, is it feasible to integrate sharing results with routine clinic visits or do they need to reach participants sooner?	6.4.7
How certain are you that the results/key messages will not change during the peer review process?	Are you confident enough that your key messages are unlikely to change substantively between presentation and publication, to share them with participants prior to publication?	6.4.7

10.8 Recommendations to improve the sharing of results with trial participants

10.8.1 Recommendations for Clinical Trials Units

To ensure trials meet their ethical obligations to participants to share trial results:

- How results will be shared with participants must be considered from the planning stage of trials, to ensure adequate resources are budgeted for and included in agreements with sites, and relevant information is included in the Patient Information Sheet
- When deciding how to share results with participants, consider the following factors: who the trial population is, the information to be communicated, who should share the results, the resources available for doing this, the tools and process for sharing results, and timing of communication
- Participants should be offered choice over whether to receive results or not
- Patient and public involvement is essential for planning how to share results with participants, identifying the outcomes and study results that are important and relevant to participants, and developing the content of results summaries to ensure it is clear and sensitively written
- Plans for sharing overall trial results should take into consideration whether this is likely to raise questions about individual results or randomised allocation, how these questions will be dealt with and by whom

10.8.2 Recommendations for research funders

To ensure people taking part in trials they fund get the chance to find out the results, if they want them, research funders should require that:

- Clinical trial grant applications specify how the research team plans to offer results to trial participants in a way that is appropriate to the study population
- Clinical trial grant applications include adequate budget to fulfil their obligation to offer the results to study participants
- Researchers report on how the results have been shared with participants who want to know them as part of their final report

10.8.3 Recommendations for ethics committees

To ensure that the trials ethics committees oversee meet their ethical obligation to offer results to participants, ethics committees should require that:

- Researchers specify how they plan to share results with participants in ethics applications
- Patient Information Sheets contain information on plans for sharing results
- Researchers report back on the implementation of these plans to ethics committees in their final report

10.9 Conclusions

For too long, clinical trials have been failing in their duty to share results with participants who want to know. This must change. While sharing results with participants is not straightforward, the Show RESPECT study shows that it can be done well, and that when it is done well, participants are glad to receive results, feel valued and find closure. Site staff are keen to be able to share results with participants, and clinical trials units must support them in this.

I conclude with words from Eva Burnett, who was a Patient Representative on the Show RESPECT Steering Group and the ICON8 Trial Management Group.

> *"Show RESPECT is one of the first studies in the UK attempting to redress the balance between the expectations and objectives of the cancer research scientific community and that of the trial patients. By having sought to find the best ways to communicate the results of the cancer study, it has placed the trial participant at its centre. It doesn't only show and commands respect towards the trial participants, as the study title indicates, but more importantly it elevates the status of the trial patient to that of a partner. In Show RESPECT study the patients are no longer passive participants.*
>
> *"The Show RESPECT study findings demonstrate that the overwhelming majority of the trial participants wish to know the outcome of the trial, even if that outcome is not of a major clinical significance. It also indicates*

that the most trial patients are genuinely interested in the meaning of their participation in the trial from the medical science development point of view. These study outcomes make me hopeful about the future of clinical research and therefore about the future of the healthcare."

11. References

1. Hariton E, Locascio JJ. Randomised controlled trials - the gold standard for effectiveness research: Study design: randomised controlled trials. BJOG. 2018;125(13):1716-.

2. Meldrum ML. A BRIEF HISTORY OF THE RANDOMIZED CONTROLLED TRIAL: From Oranges and Lemons to the Gold Standard. Hematology/Oncology Clinics of North America. 2000;14(4):745-60.

3. Medical Research Council Streptomycin in Tuberculosis Trials Committee. Streptomycin treatment for pulmonary tuberculosis. BMJ. 1948;2(4582):769-82.

4. Sertkaya A, Birkenbach A, Berlind A, Eyraud J. Examination of Clinical Trial Costs and Barriers for Drug Development Washington DC: Office of the Assistant Secretary for Planning And Evaluation, U.S. Department of Health and Human Services; 2014 [Available from: https://aspe.hhs.gov/report/examination-clinical-trial-costs-and-barriers-drug-development.

5. World Health Organisation. Number of clinical trial registrations by location, disease, phase of development, age and sex of trial participants (1999-2021): World Health Organisation; 2022 [updated February 2022; cited 2022 04/03/2022]. Available from: https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/number-of-trial-registrations-by-year-location-disease-and-phase-of-development.

6. Hudson KL, Collins FS. Sharing and reporting the results of clinical trials. JAMA : the journal of the American Medical Association. 2015;313(4):355-6.

7. Aldinger, Mary Ellen Allen, Mark Barnes, Karine Bienfait, Barbara Bierer, Juan Carmona, et al. MRCT Center Return of Individual Results Recommendations Document. Cambridge, Massachussets, USA: The MRCT Center of Brigham and Women's Hospital and Harvard; 2017 24/11/2017.

8. Taylor J. Reporting research findings to participants is an ethical imperative. BMJ. 2019;367:l6324.

9. Fernandez CV, Kodish E, Weijer C. Informing study participants of research results: an ethical imperative. IRB. 2003;25(3):12-9.

10. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA : the journal of the American Medical Association. 2013;310(20):2191-4.

11. UNAIDS, AVAC. Good participatory practice: Guidelines for biomedical HIV prevention trials. Geneva: UNIADS; 2011.

12. Health Research Authority. Information for participants at the end of a study: Guidance for Researchers/Sponsors/ Chief Investigators/Principal Investigators London: Health Research Authority; 2015 [Available from: https://s3.eu-west-2.amazonaws.com/www.hra.nhs.uk/media/documents/hra-guidance-end-study-pis-v4-1_20-august-2015.pdf.

13. Partridge AH, Wong JS, Knudsen K, Gelman R, Sampson E, Gadd M, et al. Offering participants results of a clinical trial: sharing results of a negative study. Lancet. 2005;365(9463):963-4.

14. Donaldson S, Khetani N, Maniatis G, Stephens D, Wright JG. Sharing clinical trial results with adolescent idiopathic scoliosis patients. J Pediatr Orthop. 2009;29(5):467-75.

15. Brealey S, Andronis L, Dennis L, Atwell C, Bryan S, Coulton S, et al. Participants' preference for type of leaflet used to feed back the results of a randomised trial: a survey. Trials. 2010;11:116.

16. Elzinga KE, Khan OF, Tang AR, Fernandez CV, Elzinga CL, Heng DY, et al. Adult patient perspectives on clinical trial result reporting: A survey of cancer patients. Clin Trials. 2016;13(6):574-81.

17. Baylor A, Muzoora C, Bwana M, Kembabazi A, Haberer JE, Matthews LT, et al. Dissemination of research findings to research participants living with HIV in rural Uganda: challenges and rewards. PLoS Med. 2013;10(3):e1001397.

18. Shalowitz DI, Miller FG. Communicating the results of clinical research to participants: attitudes, practices, and future directions. PLoS Med. 2008;5(5):e91.

19. Partridge AH, Wolff AC, Marcom PK, Kaufman PA, Zhang L, Gelman R, et al. The impact of sharing results of a randomized breast cancer clinical trial with study participants. Breast cancer research and treatment. 2009;115(1):123-9.

20. Williams SL, Ferrigno L, Maraini G, Rosmini F, Sperduto RD. A post-trial survey to assess the impact of dissemination of results and unmasking on participants in a 13-year randomised controlled trial on age-related cataract. Trials. 2011;12:148.

21. Buchwald H, Fitch LL, Matts JP, Johnson JW, Hansen BJ, Stuenkel MR, et al. Perception of quality of life before and after disclosure of trial results: a report from the Program on the Surgical Control of the Hyperlipidemias (POSCH). Control Clin Trials. 1993;14(6):500-10.

22. Partridge AH, Hackett N, Blood E, Gelman R, Joffe S, Bauer-Wu S, et al. Oncology physician and nurse practices and attitudes regarding offering clinical trial results to study participants. J Natl Cancer Inst. 2004;96(8):629-32.

23. Keys JR, Monk JA, Woolley KL. Sharing Results with Clinical Trial Participants: Insights from an Online Survey of Chinese Consumers. Chinese Medical Journal. 2016;129(8):1007-8.

24. Health Research Authority. Make it public: Research transparency annual report 2021. London: Health Research Authority; 2021.

25. Schroter S, Price A, Malicki M, Richards T, Clarke M. Frequency and format of clinical trial results dissemination to patients: a survey of authors of trials indexed in PubMed. BMJ Open. 2019;9(10):e032701.

26. Raza MZ, Bruhn H, Gillies K. Dissemination of trial results to participants in phase III pragmatic clinical trials: an audit of trial investigators intentions. BMJ Open. 2020;10(1):e035730.

27. Bruhn H, Cowan E-J, Campbell MK, Constable L, Cotton S, Entwistle V, et al. Providing trial results to participants in phase III pragmatic effectiveness RCTs: a scoping review. Trials. 2021;22(1):361.

28. Rigby H, Fernandez CV. Providing research results to study participants: support versus practice of researchers presenting at the American Society of Hematology annual meeting. Blood. 2005;106(4):1199-202.

29. Kozanczyn C, Collins K, Fernandez CV. Offering results to research subjects: U.S. Institutional Review Board policy. Accountability in research. 2007;14(4):255-67.

30. Macneil SD, Fernandez CV. Informing research participants of research results: analysis of Canadian university based research ethics board policies. Journal of medical ethics. 2006;32(1):49-54.

31. Hinds PS. Sharing our research findings with study participants. Cancer nursing. 2008;31(3):173-4.

32. Aldinger C, Bierer B, Collyar D, Li R, Myers L. MRCT Return of Results Guidance Document. The Multi-regional Clinical Trials Center of Brigham and Women's Hospital and Harvard; 2016 13 July 2016.

33. Chakradhar S. Many returns: call-ins and breakfasts hand back results to study volunteers. Nat Med. 2015;21(4):304-6.

34. Partridge AH, Winer EP. Informing clinical trial participants about study results. JAMA : the journal of the American Medical Association. 2002;288(3):363-5.

35. MacNeil SD, Fernandez CV. Attitudes of research ethics board chairs towards disclosure of research results to participants: results of a national survey. Journal of medical ethics. 2007;33(9):549-53.

36. Fernandez CV, Kodish E, Shurin S, Weijer C. Offering to return results to research participants: attitudes and needs of principal investigators in the Children's Oncology Group. Journal of pediatric hematology/oncology. 2003;25(9):704-8.

37. Dixon-Woods M, Tarrant C, Jackson CJ, Jones DR, Kenyon S. Providing the results of research to participants: a mixed-method study of the benefits and challenges of a consultative approach. Clin Trials. 2011;8(3):330-41.

38. Di Blasi Z, Kaptchuk TJ, Weinman J, Kleijnen J. Informing participants of allocation to placebo at trial closure: Postal survey. BMJ: British Medical Journal. 2002;325(7376):1329-31.

39. Cox K, Moghaddam N, Bird L, Elkan R. Feedback of trial results to participants: a survey of clinicians' and patients' attitudes and experiences. European journal of oncology nursing : the official journal of European Oncology Nursing Society. 2011;15(2):124-9.

40. Darbyshire JL, Holman RR, Price HC. Presenting the results of clinical trials to participants. Clinical medicine (London, England). 2009;9(5):415-6.

41. Fernandez CV, Gao J, Strahlendorf C, Moghrabi A, Pentz RD, Barfield RC, et al. Providing research results to participants: attitudes and needs of adolescents and parents of children with cancer. J Clin Oncol. 2009;27(6):878-83.

42. Getz K, Hallinan Z, Simmons D, Brickman MJ, Jumadilova Z, Pauer L, et al. Meeting the obligation to communicate clinical trial results to study volunteers. Expert Rev Clin Pharmacol. 2012;5(2):149-56.

43. Dalal H, Wingham J, Pritchard C, Northey S, Evans P, Taylor RS, et al. Communicating the results of research: how do participants of a cardiac rehabilitation RCT prefer to be informed? Health expectations : an international journal of public participation in health care and health policy. 2010;13(3):323-30.

44. Dorsey ER, Beck CA, Adams M, Chadwick G, de Blieck EA, McCallum C, et al. Communicating clinical trial results to research participants. Archives of neurology. 2008;65(12):1590-5.

45. Long CR, Stewart MK, Cunningham TV, Warmack TS, McElfish PA. Health research participants' preferences for receiving research results. Clin Trials. 2016;13(6):582-91.

46. Dixon-Woods M, Jackson C, Windridge KC, Kenyon S. Receiving a summary of the results of a trial: qualitative study of participants' views. BMJ. 2006;332(7535):206-10.

47. Snowdon C, Garcia J, Elbourne D. Reactions of participants to the results of a randomised controlled trial: exploratory study. BMJ. 1998;317(7150):21-6.

48. Mancini J, Genre D, Dalenc F, Ferrero JM, Kerbrat P, Martin AL, et al. Participants' uptake of clinical trial results: a randomised experiment. Br J Cancer. 2010;102(7):1081-4.

49. Aldinger CE, Ligibel J, Shin IH, Denninger JW, Bierer BE. Returning aggregate results of clinical trials: Empirical data of patient preferences. Journal of Clinical and Translational Science. 2018;2(6):356-62.

50. Avins AL, Bent S, Padula A, Staccone S, Badua E, Goldberg H. Initial experience with a group presentation of study results to research participants. Trials. 2008;9(1):16.

51. Scott SM, Ashford JM, Clark KN, Martin-Elbahesh K, Conklin HM. Returning research results: caregivers' reactions following computerized cognitive training among childhood cancer survivors. Neuro-Oncology Practice. 2018;5(3):194-200.

52. Getz K, Ouellette E, Simmons D, Morrison BWMD, Scott N, Wilenzick M, et al. Providing Results to Volunteers. Applied Clinical Trials. 2010;19(10):52-9.

53. Locock L, Smith L. Personal experiences of taking part in clinical trials – A qualitative study. Patient education and counseling. 2011;84(3):303-9.

54. MacNeil SD, Fernandez CV. Offering results to research participants. BMJ. 2006;332(7535):188-9.

55. Snowdon C, Brocklehurst P, Tasker R, Ward Platt M, Harvey S, Elbourne D. Death, bereavement and randomised controlled trials (BRACELET): a methodological study of policy and practice in neonatal and paediatric intensive care trials. Health Technol Assess. 2014;18(42):1-410.

56. Bierer B, Collyar D, Digilova A, Li R, Myers L, Plummer MA, et al. MRCT Return of Results Guidance Document. The Multi-regional Clinical Trials Center of Brigham and Women's Hospital and Harvard; 2015 19 March 2015.

57. Aldinger C, B B, Collyar D, Li R, Myers L. MRCT Return of Results Guidance Document. The Multi-regional Clinical Trials Center of Brigham and Women's Hospital and Harvard; 2017 22 November 2017.

58. Expert group on clinical trials for the implementation of regulation (EU) No 536/2014 on clinical trials on medicinal products for human use. Summaries of Clinical Trial Results for Laypersons. Brussels, Belgium: European Commission; 2018.

59. CISCRP. Trial results summaries Boston, MA, USA: CISCRP; 2021 [Available from: https://www.ciscrp.org/services/health-communication-services/trial-result-summaries/.

60. Bruhn H, Campbell M, Entwistle V, Humphreys R, Jayacodi S, Knapp P, et al. What, how, when and who of trial results summaries for trial participants: stakeholder-informed guidance from the RECAP project. BMJ Open. 2022;12(3):e057019.

61. Nutbeam D. Health Promotion Glossary. In: Division of Health Promotion EaCH, (HEP) HEaHPU, editors. Geneva, Switzerland: World Health Organisation; 1998. p. 36.

62. National Literacy Trust. What is literacy? : National Literacy Trust; 2017 [cited 2021 16 December 2021]. Available from: https://literacytrust.org.uk/information/what-is-literacy/.

63. National Literacy Trust. Adult literacy London: National Literacy Trust; 2017 [Available from: https://literacytrust.org.uk/parents-and-families/adult-literacy/.

64. Kutner M, Greenberg E, Jin Y, Paulsen C. The Health Literacy of America's Adults: Results from the 2003 National Assessment of Adult Literacy. In: Education USDo, editor. Washington D.C., USA: National Center for Education Statistics; 2006. p. 76.

65. Harwood A, Harrison JE. How Readable Are Orthodontic Patient Information Leaflets? Journal of Orthodontics. 2004;31(3):210-9.

66. Fausset CB, Rogers WA. Comprehension of health risk probabilities: The roles of age, numeracy, format, and mental representation. 2012;3531701:149.

67. Golbeck AL, Ahlers-Schmidt CR, Paschal AM, Dismuke SE. A Definition and Operational Framework for Health Numeracy. American Journal of Preventive Medicine. 2005;29(4):375-6.

68. Rowlands G, Protheroe J, Winkley J, Richardson M, Seed PT, Rudd R. A mismatch between population health literacy and the complexity of health information: an observational study. Br J Gen Pract. 2015;65(635):e379-86.

69. An act to enhance citizen access to Government information and services by establishing that Government documents issued to the public must be written clearly, and for other purposes., Pub. L. No. Public Law 111-274 Stat. H.R. 946 (13 October 2010, 2010).

70. Kim EJ, Kim SH. Simplification improves understanding of informed consent information in clinical trials regardless of health literacy level. Clin Trials. 2015;12(3):232-6.

71. Yates K, Pena A. Comprehension of discharge information for minor head injury: a randomised controlled trial in New Zealand. N Z Med J. 2006;119(1239):U2101.

72. Sudore RL, Landefeld CS, Barnes DE, Lindquist K, Williams BA, Brody R, et al. An advance directive redesigned to meet the literacy level of most adults: a randomized trial. Patient education and counseling. 2007;69(1-3):165-95.

73. Bunge M, Muehlhauser I, Steckelberg A. What constitutes evidence-based patient information? Overview of discussed criteria. Patient Education and Counseling. 2010;78(3):316-28.

74. National Health Service. Content style guide: how we write UK: National Health Service; 2019 [cited 2021 22/12/2021]. Available from: https://service-manual.nhs.uk/content/how-we-write.

75. Plain English Campaign. How to write in plain English High Peak: Plain English Campaign; 2009 [cited 2021 22/12/2021]. Available from: http://www.plainenglish.co.uk/files/howto.pdf.

76. Peters E, Västfjäll D, Slovic P, Mertz CK, Mazzocco K, Dickert S. Numeracy and decision making. Psychol Sci. 2006;17(5):407-13.

77. Hoffrage U, Lindsey S, Hertwig R, Gigerenzer G. Communicating Statistical Information. Science. 2000;290(5500):2261-2.

78. Knapp P, Gardner PH, Woolf E. Combined verbal and numerical expressions increase perceived risk of medicine side-effects: a randomized controlled trial of EMA recommendations. Health Expectations. 2016;19(2):264-74.

79. Edwards A, Elwyn G, Mulley A. Explaining risks: turning numerical data into meaningful pictures. BMJ (Clinical research ed). 2002;324(7341):827-30.

80. Harmsen CG, Kristiansen IS, Larsen PV, Nexøe J, Støvring H, Gyrd-Hansen D, et al. Communicating risk using absolute risk reduction or prolongation of life formats: cluster-randomised trial in general practice. British Journal of General Practice. 2014;64(621):e199.

81. Whiting PF, Sterne JAC, Westwood ME, Bachmann LM, Harbord R, Egger M, et al. Graphical presentation of diagnostic information. BMC medical research methodology. 2008;8:20-.

82. Zikmund-Fisher BJ, Ubel PA, Smith DM, Derry HA, McClure JB, Stark A, et al. Communicating side effect risks in a tamoxifen prophylaxis decision aid: the debiasing influence of pictographs. Patient education and counseling. 2008;73(2):209-14.

83. Hawley ST, Zikmund-Fisher B, Ubel P, Jancovic A, Lucas T, Fagerlin A. The impact of the format of graphical presentation on health-related knowledge and treatment choices. Patient Education and Counseling. 2008;73(3):448-55.

84. Muscatello DJ, Searles A, Macdonald R, Jorm L. Communicating population health statistics through graphs: a randomised controlled trial of graph design interventions. BMC Medicine. 2006;4(1):33.

85. O'Keefe DJ, Jensen JD. The relative persuasiveness of gain-framed and loss-framed messages for encouraging disease prevention behaviors: a meta-analytic review. Journal of health communication. 2007;12(7):623-44.

86. Plain English Campaign. Guide to design and layout UK: Plain English Campaign; 2009 [cited 2022 11/01/2022]. Available from: http://www.plainenglish.co.uk/files/designguide.pdf.

87. Knapp P, Raynor DK, Silcock J, Parkinson B. Can user testing of a clinical trial patient information sheet make it fit-for-purpose? - A randomized controlled trial. BMC Medicine. 2011;9 (no pagination)(89).

88. South A, Hanley B, Gafos M, Cromarty B, Stephens R, Sturgeon K, et al. Models and impact of patient and public involvement in studies carried out by the Medical Research Council Clinical Trials Unit at University College London: findings from ten case studies. Trials. 2016;17:376.

89. Gafos M, South A, Hanley B, Brodnicki E, Hodson M, McCormack S, et al. "PROUD to have been involved": an evaluation of participant and community involvement in the PROUD HIV prevention trial. Research Involvement and Engagement. 2020;6(1):13.

90. Brett J, Staniszewska S, Mockford C, Herron-Marx S, Hughes J, Tysall C, et al. Mapping the impact of patient and public involvement on health and social care research: a systematic review. Health expectations : an international journal of public participation in health care and health policy. 2014;17(5):637-50.

91. Montgomery AA, Peters TJ, Little P. Design, analysis and presentation of factorial randomised controlled trials. BMC Med Res Methodol. 2003;3:26.

92. Clamp AR, James EC, McNeish IA, Dean A, Kim JW, O'Donnell DM, et al. Weekly dose-dense chemotherapy in first-line epithelial ovarian, fallopian tube, or primary peritoneal carcinoma treatment (ICON8): primary progression free survival analysis results from a GCIG phase 3 randomised controlled trial. Lancet. 2019;394(10214):2084-95.

93. John. S, Broggio J. Cancer survival in England - adults diagnosed. In: Office for National Statistics, editor. 2013-2017 edition ed. UK2019.

94. Hemming K, Eldridge S, Forbes G, Weijer C, Taljaard M. How to design efficient cluster randomised trials. BMJ. 2017;358:j3064.

95. Teddlie C, Tashakkori A. A general typology of research designs featuring mixed methods. Research in the Schools. 2006;13(1):12-28.

96. Moran-Ellis J, Alexander VD, Cronin A, Dickinson M, Fielding J, Sleney J, et al. Triangulation and integration: processes, claims and implications. Qualitative Research. 2006;6(1):45-59.

97. Farmer T, Robinson K, Elliott SJ, Eyles J. Developing and Implementing a Triangulation Protocol for Qualitative Health Research. Qualitative Health Research. 2006;16(3):377-94.

98. Archer M, Decoteau C, Gorski P, Little D, Porpora D, Rutzou T, et al. What is Critical Realism? Perspectives: A Newsletter of the AS Theory Section. 2016.

99. Vincent S, O'Mahoney J. Critical Realism and Qualitative Research: An introductory Overview. In: C. Cassell, A. L. Cunliffe, G. Grandy, editors. The SAGE handbook of qualitative business and management research methods SAGE Publications Ltd; 2018. p. 201-16.

100. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. Qualitative Health Research. 2015;26(13):1753-60.

101. National Institute for Health and Care Excellence. The Guidelines Manual: Process and methods [PMG6]: Appendix H: Methodology checklist: qualitative studies London: National Institute for Health and Care Excellence,; 2021 [Available from: https://www.nice.org.uk/process/pmg6/resources/the-guidelines-manual-appendices-bi-2549703709/chapter/appendix-h-methodology-checklist-qualitative-studies.

102. Guest G, Namey E, Mitchell M. Chapter 1: Qualitative Research: Defining and Designing. 2013 2021/03/24. In: Collecting Qualitative Data: A Field Manual for Applied Research [Internet]. 55 City Road, London: SAGE Publications, Ltd. Available from: https://methods.sagepub.com/book/collecting-qualitative-data.

103. Bailey J. First steps in qualitative data analysis: transcribing. Fam Pract. 2008;25(2):127-31.

104. Braun V, Clarke V. Reflecting on reflexive thematic analysis. Qualitative Research in Sport, Exercise and Health. 2019;11(4):589-97.

105. Robson A, Robinson L. Building on models of information behaviour: linking information seeking and communication. J Doc. 2013;69(2):169-93.

106. Robson A, Robinson L. The Information Seeking and Communication Model. J Doc. 2015;71(5):1043-69.

107. Office for National Statistics. Exploring the UK's digital divide. Office for National Statistics; 2019 04/03/2019.

108. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ : British Medical Journal. 2014;348:g1687.

109. Health Research Authority. Information for participants at the end of a study: Guidance for Researchers /Sponsors/ Chief Investigators/Principal Investigators. In: Authority HR, editor.: Health Research Authority; 2015.

110. South A, Joharatnam-Hogan N, Purvis C, James EC, Diaz-Montana C, Cragg WJ, et al. Testing approaches to sharing trial results with participants: The Show RESPECT cluster randomised, factorial, mixed methods trial. PLoS Medicine. 2021;18(10).

111. Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. Quality & Quantity. 2018;52(4):1893-907.

112. Eccles DW, Arsal G. The think aloud method: what is it and how do I use it? Qualitative Research in Sport, Exercise and Health. 2017;9(4):514-31.

113. Spears MR, James ND, Sydes MR. 'Thursday's child has far to go'-interpreting subgroups and the STAMPEDE trial. Ann Oncol. 2017;28(10):2327-30.

114. Rothwell PM. Subgroup analysis in randomised controlled trials: importance, indications, and interpretation. The Lancet. 2005;365(9454):176-86.

115. Institute of Medicine (US) Committee on Health Literacy. Health Literacy: A prescription to end confusion. Washington DC: National Academies Press (US); 2004.

116. CISCRP. Perceptions & Insights Study: Report on Study Participant Experiences. Boston, MA: CISCRP; 2013.

117. Wood J, Cotton SC, Gillies K. The relative importance of information items and preferred mode of delivery when disseminating results from trials to participants: A mixed-methods study. Health Expectations. 2022;25(1):419-29.

118. Racine E, Hurley C, Cheung A, Sinnott C, Matvienko-Sikar K, Baumgartner C, et al. Participants' perspectives and preferences on clinical trial result dissemination: The TRUST Thyroid Trial experience [version 2; peer review: 2 approved]. HRB Open Research. 2019;1(14).

119. Fernandez CV, Kodish E, Weijer C. Importance of informed consent in offering to return research results to research participants. Medical and pediatric oncology. 2003;41(6):592-3.

120. Trialists should tell participants results, but how? Lancet. 2006;367(9516):1030.

121. Naidoo N, Nguyen VT, Ravaud P, Young B, Amiel P, Schanté D, et al. The research burden of randomized controlled trial participation: a systematic thematic synthesis of qualitative evidence. BMC medicine. 2020;18(1):6.

122. Lawton J, Blackburn M, Breckenridge JP, Hallowell N, Farrington C, Rankin D. Ambassadors of hope, research pioneers and agents of change—individuals' expectations and experiences of taking part in a randomised trial of an innovative health technology: longitudinal qualitative study. Trials. 2019;20(1):289.

123. Sheridan R, Martin-Kerry J, Hudson J, Parker A, Bower P, Knapp P. Why do patients take part in research? An overview of systematic reviews of psychosocial barriers and facilitators. Trials. 2020;21(1):259.

124. Partridge AH, Winer EP. Sharing study results with trial participants: time for action. J Clin Oncol. 2009;27(6):838-9.

125. Ellis A, Scroggins MJ. Patient perspectives on clinical trial participation: A pilot survey of gynecologic cancer survivors. Gynecologic Oncology. 2020;159:250-1.

126. von Wagner C, Knight K, Steptoe A, Wardle J. Functional health literacy and health-promoting behaviour in a national sample of British adults. J Epidemiol Community Health. 2007;61(12):1086-90.

127. Dani KA, Stobo DB, Capell HA, Madhok R. Audit of literacy of medical patients in north Glasgow. Scott Med J. 2007;52(2):21-4.

128. Flesch R. A new readability yardstick. J Appl Psychol. 1948;32(3):221-33.

129. Flodgren G. Are Cochrane plain language summaries plain? Cochrane Colloquiem; Seoul2016.

130. Bruhn H, Anderson AS, Hickman A, Macaskill EJ, Treweek S. Letter on "Sharing trial results directly with trial participants and other stakeholders after the SARS-CoV-2 pandemic hit the UK – experience from the ActWELL trial". Trials. 2021;22(1):381.

131. Pirosca S, Shiely F, Clarke M, Treweek S. Tolerating bad health research: the continuing scandal. Trials. 2022;23(1):458.

132. Thackeray R, Neiger BL. A Multidirectional Communication Model: Implications for Social Marketing Practice. Health Promotion Practice. 2009;10(2):171-5.

133. Greenhalgh T, Bate P, Macfarlane F, Kyriakidou O. Diffusion and Dissemination. In: Greenhalgh T, Bate P, Macfarlane F, Kyriakidou O, editor. Diffusion of Innovations in Health Service Organisations: Blackwell Publishing Ltd; 2005. p. 114-33.

134. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, et al. Lost in knowledge translation: time for a map? J Contin Educ Health Prof. 2006;26(1):13-24.

135. Murray E, Treweek S, Pope C, MacFarlane A, Ballini L, Dowrick C, et al. Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. BMC Medicine. 2010;8(1):63.

136. Atkins L, Francis J, Islam R, O'Connor D, Patey A, Ivers N, et al. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. Implementation Science. 2017;12(1):77.

137. Salterio SE, Hoang K, Luo Y. Communication is a two-way street: Analyzing practices undertaken to systematically transfer audit research knowledge to policymakers. Accounting Organizations and Society. 2021;94:101265.

138. Ahmadinia H, Eriksson-Backa K, Nikou S. Health-seeking behaviours of immigrants, asylum seekers and refugees in Europe: a systematic review of peer-reviewed articles. Journal of Documentation. 2021;78(7):18-41.

139. Rutkowski RA, Ponnala S, Younan L, Weiler DT, Bykovskyi AG, Werner NE. A process-based approach to exploring the information behavior of informal caregivers of people living with dementia. International Journal of Medical Informatics. 2020;145:104341.

140. Association for Measurement and Evaluation of Communication. Integrated Evaluation Framework: Association for Measurement and Evaluation of Communication; 2016 [Available from: https://amecorg.com/amecframework/framework/interactive-framework/.

141. NHS Digital. NHS DigiTrials: NHS Digital; 2022 [updated 31/01/2022; cited 2022 24/06/22]. Available from: https://digital.nhs.uk/services/nhs-digitrials.

Annex 1: Patient questionnaire

ICON8 Trial Results Feedback Questionnaire

Show Results to Participants Engaged in Clinical Trials (Show RESPECT)

ICON8 Trial Number: | | | | | | | | | Year of birth: y y y y

Before you start, please check the year of birth above - is this right? If the year of birth above is correct, please continue to question 1. If not, please do not complete this questionnaire yet as you may not have the right questionnaire for you. Please contact your ICON8 nurse to check if the trial number above is your ICON8 trial number.

1. What is today's date? d d m m m y y y y

This information will help us understand if different people have different preferences about how to receive trial results.

Section 1: About you

2. Is English your first language? Yes ☐ No ☐

3. What is your highest level of education?

- ☐ No qualifications
- ☐ GCSE / O-level / NVQ level 1 / Foundation Diploma / equivalent
- ☐ A-level / CSE / NVQ level 2 / Intermediate or Higher Diploma / equivalent
- ☐ Undergraduate degree
- ☐ Postgraduate degree

4. How often do you use the internet or email?

- ☐ Never
- ☐ Once per month at most
- ☐ More than once per month, but not as often as every week
- ☐ Once per week or more, but not as often as every day
- ☐ Every day

ICON8 Trial Number: | | | | | | | | |

Section 2: Finding out about the results of the trial

5a. Did you/do you want to find out the results of the ICON8 trial? Yes ☐ No ☐

5b. If no, could you explain why not? (If you did, go to question 6).

……

……

……

6a. Have you found out about the results of the ICON8 trial? Yes ☐ No ☐

The table below shows the different ways we offered you to find out about the ICON8 trial results. We would like to know how you felt about these.

Ways we offered you to find out about the ICON8 results:	**Webpage**	**Printed summary in the post**	**An invitation to join an email mailing list**
6b. Do you remember being offered or given?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
6c. Did you use these?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
6d. Tick one way which you preferred receiving the results.	☐	☐	☐

7a. Did you find out about the results in any other way(s)? Yes ☐ No ☐

7b. If yes, which other ways? (If no, go to question 8)

……

……

8a. Are there other ways you would have liked to receive the results? Yes ☐ No ☐

8b. If yes, how? (If no, go to question 9)

……

……

9a. How satisfied are you with the <u>way</u> you found out the results of ICON8 (rather than the results themselves)?



Very unsatisfied	Quite unsatisfied	Neither satisfied nor unsatisfied	Quite satisfied	Very satisfied
☐	☐	☐	☐	☐

9b. What were the main reason(s) why you were satisfied or unsatisfied?

.....

.....

.....

Section 3: The information you received

For each of the following statements, please tick the box that best matches how you feel.

10a. The information about the trial results told me everything I wanted to know.

Strongly disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Strongly agree
☐	☐	☐	☐	☐

10b. If the information did not tell you everything you wanted to know, what was missing?

.....

.....

.....

11. The ICON8 trial results were easy to understand.

Strongly disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Strongly agree
☐	☐	☐	☐	☐

12. It was easy for me to find out the ICON8 trial results.

Strongly disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Strongly agree
☐	☐	☐	☐	☐

ICON8 Trial Number: | | | | | | | | |

Section 4: How the results made you feel

For each of the following statements, please tick the box that best matches how you feel.

13. I am glad I found out the results.

Strongly disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Strongly agree
☐	☐	☐	☐	☐

14. I regret finding out the results.

Strongly disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Strongly agree
☐	☐	☐	☐	☐

15. I found the results upsetting to hear about.

Strongly disagree	Slightly disagree	Neither agree nor disagree	Slightly agree	Strongly agree
☐	☐	☐	☐	☐

Section 5: How you feel about research participation

For each of the following statements, please tick the box that best matches how you feel.

16. How willing do you think you would be to take part in research again in future?

Very unwilling	Quite unwilling	Not sure	Quite willing	Very willing
☐	☐	☐	☐	☐

17. How likely are you to recommend research participation to friends or family?

Very unlikely	Quite unlikely	Not sure	Quite likely	Very likely
☐	☐	☐	☐	☐

Thank you for completing this questionnaire. It will help us improve how we share trial results with people like you.

Please return this questionnaire using the prepaid envelope provided.

For office use only:

Date form received at CTU: dd - mmm - yyyy

Date form entered onto database : dd - mmm - yyyy

Initials of data enterer: | | | | |

Annex 2: Site staff Case Report Forms

Show RESPECT Site Feedback Questionnaire
Show Results to Participants Engaged in Clinical Trials
Form 2A

ICON8 Site Number: ☐☐☐ Site Name……..

Study Number: ☐☐☐☐☐☐☐☐

Introduction

Please **only** complete this form if you were involved in the distribution of the Printed Summary and/or the Patient Update Information sheet to participants.

Please ask your site's main ICON8 trial contact to record that you have completed this questionnaire by entering your name next to the site questionnaire number, given above, on the **site feedback questionnaire log**. This will not be sent to MRC CTU at UCL, so your completion of this questionnaire will remain confidential.

1. What is today's date? d d m m m y y y y

2. What are your initials? ☐☐☐☐

Section 1—About you

This information will help us understand if different people have different views about how to share trial results.

3a. Which of the following most closely matches your current job role?

- ☐ Research nurse, research practitioner, research radiologist, clinical nurse specialist
- ☐ Clinician
- ☐ Clinical trial coordinator or research manager
- ☐ Data manager
- ☐ Trials administrator
- ☐ Other, b. please specify……..

4. How long have you worked in clinical trials?

Less than 1 year	1 year to 5 years	6 to 10 years	Over 10 years
☐	☐	☐	☐

5. How many trials do you work on now?

1-5	6-10	Over 10
☐	☐	☐

ICON8 Site Number: ☐☐☐ Site Name……

Study Number: ☐☐☐☐☐☐☐☐

6. Approximately how much of your time do you currently spend on ICON8?

Almost none	Around one day per week	Around two days per week	Three or more days per week
☐	☐	☐	☐

7. Approximately how long have you worked on the ICON8 trial?

Less than 1 year	1-2 years	3-4 years	5 or more years
☐	☐	☐	☐

8a. What has/will be your involvement been in sharing the ICON8 results? Tick all that apply.

☐ Sending the Printed Summary and/or the Patient Update Information sheet to patients by post

☐ Handling or answering queries from patients about the trial results

☐ Other, b. please specify ……

Section 2—Time and resource needed to send out results

9. Approximately how many hours did it take to send out the ICON8 Patient Update Information Sheet to all participants?

0-1	2-4	5-7	8-10	More than 10
☐	☐	☐	☐	☐

10. Approximately how many hours did it take to send out the Printed Summary to all participants?

0-1	2-4	5-7	8-10	More than 10
☐	☐	☐	☐	☐

11. What costs did your hospital incur for sending out the Printed Summary to participants, if any (excluding staff time)?

……

ICON8 Site Number: | | | | Site Name……

Study Number: | | | | | | | | |

Section 3—Your views

12a. Which approach do you prefer for sharing results with participants? (Please tick one box)

- ☐ Posted, printed summary
- ☐ Email
- ☐ Basic webpage
- ☐ Enhanced webpage (i.e. with videos and other extra content)
- ☐ Combination of approaches, b. please specify……
- ☐ Other, b. please specify……

13. Why do you think this/these method(s) are the best…… …..

……..

……...

14a. Do you have any concerns about how you shared the ICON8 results with participants?

Yes ☐ No ☐

14b. If so, please explain why…… …..

……..

15a. Was anything challenging about sharing the ICON8 results?

Yes ☐ No ☐

15b. If so, please explain:……..

……...

……...

Show RESPECT Site Feedback Questionnaire
Show Results to Participants Engaged in Clinical Trials
Form 2A

ICON8 Site Number: | | | | Site Name……..

Study Number: | | | | | | | | |

16a. Do you think the way(s) you shared results should be standard practice for trials you are involved in?

Yes ☐ No ☐

16b. If so, which method? And why? ……

……

……..

17a. Would you do anything differently for future trials whose results you are involved in communicating?

Yes ☐ No ☐

17b. If so, what would you do differently?……

……

……..

ICON8 Site Number: | | | | Site Name……..

Study Number: | | | | | | | | |

Introduction

Please **only** complete this form if you were involved in the handling or answering queries from participants about the trial results.

Please ask your site's main ICON8 trial contact to record that you have completed this questionnaire by entering your name next to the site questionnaire number, given above, on the **site feedback questionnaire log**. This will not be sent to MRC CTU at UCL, so your completion of this questionnaire will remain confidential.

1. What is today's date? | d | d | m | m | m | y | y | y | y |

2. What are your initials | | | | |

Section 1—About you

This information will help us understand if different people have different views about how to share trial results.

3a. Which of the following most closely matches your current job role?

- ☐ Research nurse, research practitioner, research radiologist, clinical nurse specialist
- ☐ Clinician
- ☐ Clinical trial coordinator or research manager
- ☐ Data manager
- ☐ Trials administrator
- ☐ Other, b. please specify……..

4. How long have you worked in clinical trials?

Less than 1 year	1 year to 5 years	6 to 10 years	Over 10 years
☐	☐	☐	☐

5. How many trials do you work on now?

1-5	6-10	Over 10
☐	☐	☐

ICON8 Site Number: ☐☐☐ Site Name……

Study Number: ☐☐☐☐☐☐☐☐

6. Approximately how much of your time do you currently spend on ICON8?

Almost none	Around one day per week	Around two days per week	Three or more days per week
☐	☐	☐	☐

7. Approximately how long have you worked on the ICON8 trial?

Less than 1 year	1-2 years	3-4 years	5 or more years
☐	☐	☐	☐

8a. What has your involvement been in sharing the ICON8 results? Tick all that apply.

☐ Sending the Printed Summary or the Patient Update Information sheet to patients by post

☐ Handling or answering queries from patients about the trial results

☐ Other, b. please specify ……

Section 2—Participant responses

9. How many participants do you remember contacting you (by any means) with queries about the results?

1-2	3-5	5-10	More than 10
☐	☐	☐	☐

10. Approximately how many hours have you spent dealing with participant queries about the ICON8 trial results?

0-1	2-4	5-7	8-10	More than 10
☐	☐	☐	☐	☐

ICON8 Site Number: ☐☐☐ Site Name……

Study Number: ☐☐☐☐☐☐☐☐

11. How able did you feel to help with participant queries?

It was very difficult to help	It was quite difficult to help	Not sure	It was quite easy to help	It was very easy to help
☐	☐	☐	☐	☐

12. Do you remember any participants being distressed or upset about the trial results?

Yes ☐ No ☐

Section 4—Your views

13a. Which approach do you prefer for sharing results with participants? (Please tick one box)

- ☐ Posted, printed summary
- ☐ Email
- ☐ Basic webpage
- ☐ Enhanced webpage (i.e. with videos and other extra content)
- ☐ Combination of approaches, b. please specify……
- ☐ Other, b. please specify……

14. Why do you think this/these method(s) are the best?

……

……

15a. Do you have any concerns about how you shared the ICON8 results with participants?

Yes ☐ No ☐

15b. If so, please explain why……

……

MRC Clinical Trials Unit

Show RESPECT Site Feedback Questionnaire
Show Results to Participants Engaged in Clinical Trials
Form 3

UCL

ICON8 Site Number: | | | | Site Name……

Study Number: | | | | | | | | |

16a. Was anything challenging about sharing the ICON8 results?

Yes ☐ No ☐

16b. If so, please explain: ……..

……...

17a. Do you think the way(s) you shared results should be standard practice for trials you are involved in?

Yes ☐ No ☐

17b. If so, which method? And why? ……

……

……...

18a. Would you do anything differently for future trials whose results you are involved in communicating?

Yes ☐ No ☐

18b. If so, what would you do differently?……

……

……...

Annex 2

Annex 3: Clinical Trials Unit staff Case Report Forms

Show RESPECT MRC CTU at UCL Questionnaire
Show Results to Participants Engaged in Clinical Trials
Form 4

Study Number: | | | | | | | | |

Introduction

We would like you to complete two questionnaires so that we can find out more about the experiences of staff at the MRC CTU at UCL in developing the methods used to distribute the ICON8 trial results to participants. We anticipate both questionnaires will take around 5 minutes to complete. You do not have to complete them, but if you do, we would be very grateful, and you will be helping us understand how best to share trial results in future. The results of these questionnaire will be included in a peer-reviewed publication, and individuals will not be identifiable.

This questionnaire will be completed after the development of the methods to distribute the results, and second will be completed after the methods have been distributed to record details of any queries from sites or participants.

1. What is today's date? | d | d | m | m | m | y | y | y | y |

2. What are your initials | | | | | (We would like to collect this only to allow us to link this questionnaire to the second questionnaire.)

Section 1. Time taken to develop the trial results materials

Please complete the table below to indicate how many hours <u>you</u> spent working on each stage of development for each method of sharing the results. (Please complete each column)

Stage	Approximate hours taken	a. Patient Update Information Sheet	b. Basic webpage	c. Enhanced webpage	d. Email newsletter	e. Printed results summary
3. Initial development	0					
	1-3					
	4-7					
	8-10					
	More than 10					
4. Testing and/ or review	0					
	1-3					
	4-7					
	8-10					
	More than 10					

For office use only:
Date form received at CTU: dd - mmm - yyyy
Date form entered onto database : dd - mmm - yyyy
Initials of data enterer: | | | | |

Show RESPECT MRC CTU at UCL Questionnaire
Show Results to Participants Engaged in Clinical Trials
Form 5

Study Number: | | | | | | | | |

Introduction

This second questionnaire is about disseminating the ICON8 trial results and should be completed around **2-3 months** after the Patient Update Information Sheet has been sent to ICON8 trial participants. We will ask about any responses received from sites and participants, and then your views about the process. We anticipate this second questionnaire will take less than **5** minutes. The results of these questionnaire will be included in a peer-reviewed publication, and individuals will not be identifiable.

1. What is today's date? d d m m m y y y y

2. What are your initials | | | | (We would like to collect this only to allow us to link this questionnaire to the first questionnaire.)

Section 1. Time taken to distribute trial result materials

Please complete the table below to indicate how many hours <u>you</u> spent working on disseminating each method of results. (Please complete each column)

Stage	Approximate hours taken	a. Patient Update Information Sheet	d. Email newsletter	e. Printed results summary
3. Disseminating to sites or participants	0			
	1-3			
	4-7			
	8-10			
	More than 10			

Section 2. Site and participant responses

4. How many sites do you remember contacting you (by any means) with queries about the methods used to distribute the results or the results themselves?

| |

5. How many queries do you remember receiving from sites about the methods used to distribute the results or the results themselves?

| |

6. Approximately how many hours have you spent dealing with site queries about the methods used to share ICON8 trial results?

0-1 ☐ 2-4 ☐ 5-7 ☐ 8-10 ☐ More than 10 ☐

Study Number: ☐☐☐☐☐☐☐☐

Section 2. Site and participant responses continued.

7. Approximately how many hours have you spent dealing with site queries about the ICON8 trial results themselves?

0-1	2-4	5-7	8-10	More than 10
☐	☐	☐	☐	☐

8a. Did you receive any direct contact from ICON8 participants?

Yes ☐ No ☐ (If no, go to question 9.)

8b. If yes, approximately how many contacted you?

☐☐

8c. On average how long did it take to deal with each of these contacts from participants?

0-10 minutes	11-30 minutes	More than 30 minutes
☐	☐	☐

9. Approximately how many hours have you spent chasing sites to perform actions relating to sending ICON8 results to participants? (Do not include any chasing relating to collecting data for the Show RESPECT study).

N/a	Less than one hour	1-4 hours	5-8 hours	More than 1 working day
☐	☐	☐	☐	☐

Section 3. Your views

10. Which approach do you prefer for sharing results with participants? (Please tick one box)

- ☐ Posted, printed summary
- ☐ Email
- ☐ Basic webpage
- ☐ Enhanced webpage (i.e. with videos and other extra content)
- ☐ Combination of approaches, b. please specify……
- ☐ Other, b. please specify……

10c. Why do you prefer this method?

……

……

Study Number: | | | | | | | | |

Section 3. Your views continued.

11a. Do you have any concerns about how we shared the ICON8 results with participants?

Yes ☐ No ☐ (If no, go to question 12.)

11b. If yes, please explain why……

……

12a. Was anything challenging about sharing the ICON8 results?

Yes ☐ No ☐ (If no, go to question 13.)

12b. If yes, please explain: ……

……

13a. Do you think any of the ways we shared the ICON8 results should be standard practice for trials you are involved in?

Yes ☐ No ☐ (If no, go to question 14.)

13b. If yes, which method? And why? ……

……

……

14a. Would you do anything differently for future trials whose results you are involved in communicating?

Yes ☐ No ☐

14b. If yes, what would you do differently?……

……

……

Thank you for completing this questionnaire.

For office use only:

Date form received at dd - mmm - yyyy

Date form entered onto dd - mmm - yyyy

Initials of data enterer: | | | | |

Annex 4: Topic guide for patient interviews

Show RESPECT: topic guide for interviews with ICON8 participants

Research questions *[for reference, not for asking participants]*

The aim of the study is to help us find the best ways to communicate results to people in research studies, and see what lessons we can learn from how this was done in ICON8.

1. What are the experiences and views of women in the ICON8 ovarian cancer trial on how the results were communicated to them?
2. What aspects of the mode of communication influence satisfaction with how the results are communicated, and why?
3. What other factors influence how satisfied women taking part in the ICON8 trial are with how the results are communicated to them?
4. What lessons can we learn from how the ICON8 results were communicated to participants?

Introduction

- Thanks
    - For participating in ICON8
    - And for agreeing to be interviewed
- Who I am
    - I'm a researcher working at the MRC Clinical Trials Unit at UCL. We run large clinical trials on cancer and infectious diseases, including the ICON8 trial. I've been working at the Unit for 8 years, and my focus is on how we communicate the results of our trials, and how we involve patients as partners in our research.
- Go through participant info sheet
- Aim of study – to help us find the best ways to communicate results to people in research studies
    - Why I want to talk to her
    - Confidentiality and anonymity
    - Recording
    - Any questions?
- Go through consent form
- Interested in your views and experiences - no right or wrong answers.
- We can stop at any time, or take a break, or skip questions you don't want to answer

Health information sources

- When you want health information, where do you usually go for it?
    - Why?
    - Any other sources?

    - (Probe re. whether they use websites / ask people / look at medical journals for information)
- Do you usually find what you want to know?
- How would you describe your confidence at using the internet to find out information?
- Is health research and medical science something you're interested in?

Experience of being part of ICON8

Remind participant about what ICON8 was about

- How long have you been taking part in the ICON8 trial for?
- Why did you decide to take part?
- How would you describe your experience of being part of ICON8?
    - Do you feel your participation is valued by your medical team?
- When you joined ICON8, did you think you would want to know the results of the trial when they were available?
- How good do you think your ICON8 doctors and nurses are at keeping you informed about your treatment and health?
    - Do they explain things well for you?
    - Have you had any problems understanding the medical information they give you?
    - Do you feel comfortable asking them questions about your health and treatment?
- How good do you think your ICON8 doctors and nurses are at keeping you informed about the research study?
    - Do they explain things well for you?
    - Have you had any problems with understanding the information you've been given about the study?
    - Do you feel comfortable asking them questions?
    - Do you get frequent enough updates about the study?

Experience of finding out the ICON8 results

Now we're going to focus on your experience of finding out the overall ICON8 results (so not your individual test results, but the overall results of the study)

- Do you remember receiving the patient update, telling you how to find out the results? [show copy]
    - If yes, what did you think when you received it?
        - How did you feel?
    - If no, let them look at the patient update to see if it jogs their memory
        - Would you like to find out the results in any of those ways?
    - Did you want to find out the results in the first place?
        - Did that change over time?
- Do you remember finding out the results of ICON8?

- *If yes,* tell me about finding out the results of ICON8
  - How?
  - How was your health when you found out the overall results?

  Reaction to finding out the results
  - How did you feel emotionally about finding out the results?
    - Why?
    - *(Comprehension, content, respected / valued, pride, satisfaction, made a difference, disappointed, confused)*
  - Has your emotional reaction to the results changed over time?
    - If yes, in what way?
  - Do you regret finding out the overall study results, or are you glad you did?
    - If yes, Why?

- *[Look at website/printed summary/email together if either of these were how they found out the results]*
  - What do you think of it now you've seen it again?
  - What do you like or dislike about it? (prompt: look and feel, content, language, navigation, *use of diagrams, links to further support and information, video, faq section*)
  - Which bits did you look at? Was anything particularly interesting? [prompt more on this]
  - Were there particularly boring or irrelevant bits?
  - Was any of it upsetting?
  - What would you change or add?
  - Was any of it confusing or unclear?
  - What do you think of the layout and formatting?

- Were you offered any other ways of finding out the results?
  - *If yes,* Which?
    - Did you use any of those ways?
      - *[If yes]* which? Why? Tell me about it.
      - *[if not:]* Why did you decide not to use those ways?

- Would you prefer to be able to find out the results in a different way?
  - *If so, how? Why?*

- If the results had been different, do you think that would change how you would prefer to have the results communicated to you?
  - *What if having weekly chemotherapy was better?*
  - *What if having three weekly chemotherapy was better?*

Interpretation of the results

- What do you think the ICON8 results mean?
  - *Interesting? Important?*
  - *Do you think it will help other patients?*

- Did you discuss the results with anyone?
  - *If so, who?*
    - *Doctor / nurse?*
    - *Friends / family?*
  - *What did you talk about?*

- Did you have any questions about the results?

- Did you want any further information or support?
  - If so, what info or support did you want?
  - Did you seek further info or support?
    - If yes, did you get further info or support?
      - *If yes,* who or where from?

- How do the results compare to your own experience in ICON8?

- How did finding out the overall results make you feel about the group of the study you were in?

Other ways of finding out the results

Some of the other women taking part in the ICON8 trial found out the results from this webpage [show other website – give time to look at]

- What do you think of this way of finding out the ICON8 results?

- Would you have liked the option to find out this way?
  - *Why?*

- How do you think researchers could improve it?

- What do you think of the layout?

- What do you think of the content?

For those looking at enhanced webpage:

- Do you think the video is helpful?
  - *For you?*
  - *For others?*

- Do you think the links to further information and support are helpful?
  - *For you?*
  - *For others?*

- Do you think the diagrams are helpful?
  - *For you?*

- *For others?*

- Do you think being able to send in a question and have it answered on the webpage is helpful?
  - *For you?*
  - *For others?*

For women who didn't receive the printed summary:

Some of the other women taking part in the ICON8 trial were sent this printed summary through the post [give copy and time to look at]

- What do you think of this way of finding out the ICON8 results?
- Would you have liked to find out this way?
  - *Why?*
-
- What do you think about the format and layout?
- What do you think about the use of diagrams?
- What do you think about the wording?
- How do you think researchers could improve it?

For women who weren't offered the email list:

Some of the other women taking part in the ICON8 trial were able to join an email list to receive the results by email. Here's the email they were sent. [Give time to look at email]

- What do you think of this way of finding out the ICON8 results?
- Would you have liked to find out this way?
  - *Why?*
-
- What do you think about the format and layout?
- What do you think about the use of diagrams?
- What do you think about the wording?
- How do you think researchers could improve it?

Sharing the results with others

- What do you think about us sharing the overall trial results with people who weren't on the trial, but care for people on the trial?
  - Eg. relatives

    - Wider care team (eg. GP)

- What do you think we should do about sharing overall trial results where the person who was taking part in the trial has died?
    - Should we contact relatives to offer them results?
        - helpful for them to know what their loved one contributed to?
        - too upsetting?
        - How can we do it sensitively?

Final thoughts

- What advice would you give to researchers in other trials on how to share the results with participants?

- Is there anything else you'd like to say about this topic?

Thanks and wrap up

- Thank you
    - For your contribution to the ICON8 trial, and to this study
- This information will help us improve how we communicate results to trial participants
- Answer any questions they have about the ICON8 results, if these came up earlier
- Give contact details for further support if needed
- Give voucher

Annex 5: Topic guide for site staff interviews

ICON8 Site Staff topic guide version 1.2 18/06/19

Show RESPECT: topic guide for interviews with ICON8 site staff

Research questions *[for reference, not for asking participants]*

The aim of the study is to help us find the best ways to communicate results to people in research studies, and see what lessons we can learn from how this was done in ICON8.

1. What are the experiences and views of site staff in communicating the results of the ICON8 trial to the trial participants using the approaches tested in the Show RESPECT study, and how are these views shaped by their clinical setting or the interventions their site was randomised to?
2. What influences their views?
3. Which approaches to communicating trial results to participants are acceptable and feasible to implement for site staff?

Introduction

- Thanks
- Who I am
- Go through participant info sheet
  - Aim of study – to help us find the best ways to communicate results to people in research studies
    - Why I want to talk to you
    - Confidentiality and anonymity
    - Recording
    - Any questions?
- Go through consent form

Start recording

- Interested in your views and experiences - no right or wrong answers.
- We can stop at any time, or take a break, or skip questions you don't want to answer

About your role

- Please could you start by telling me your job title?
- What does that involve?
- What do you think are the most important aspects of your role?
  - *Do you have direct contact with participants?*
- What has been your role in the ICON8 study?
  - *How well do you know the participants?*
- What has been your role in the Show RESPECT study?
- How many trials do you work on?
- What diseases are the trials for?

- Do you find there are differences between the patients in the different trials in how much information they want?
    - Probe for details

Information sources

- Do you generally find out the results of the trials you work on?
- How do you generally find out the results of trials you have worked on?

Past experience of sharing trial results

- Is sharing overall trial results with participants something you do routinely?

- Do you have experience of sharing trial results with participants on previous trials? If so, please could you tell me about it?
    - *How?*
    - *When?*
    - *To whom?*
    - *Response*
        - *Has response varied b:*
            - *Trial arm*
            - *Results*
            - *Disease / stage*
    - *What support did you receive from*
        - *the CTU coordinating the trial?*
        - *Colleagues*

Views about sharing results with trial participants in general

- What are your views about sharing results with trial participants in general?
    - *Do you think participants want to know?*
    - *Do you have any concerns about it in principle?*
        - *Any exceptions/ special cases?*
            - *What if the trial shows clear benefit from the intervention?*
            - *What if the trial shows no difference?*
            - *What if the trial shows harm from the intervention?*
            - *What if there is high mortality in the trial?*
    - *What do you think the benefits of sharing results might be?*
    - *What do you think the drawbacks of sharing results might be?*
    - *Do you think your views are shared by your colleagues?*

Practicalities of sharing ICON8 results

- Could you talk me through the process you used for sharing the ICON8 results with participants?
    - *Time spent sending out the update sheet*

- *Contacting participants – did you personalise the PUIS sheets / include a cover note / ring participants?*
- *Timing*
- *Time spent sending out the printed summary (if applicable)*
- *Did you encounter any difficulties?*

- What would make it easier to share results with participants?

ICON8 Participants' responses to finding out the results

- What responses have you had from participants to being offered the ICON8 results?
  - *Questions?*

Views on how the ICON8 results were shared

Your site was randomised to offer participants:

- What do you think about these methods to communicate the ICON8 results?
  - *Which method do you prefer? If so, why?*
  - *If the results had been difference, would that change which method you think should be used?*
    - *Showed clear benefit from weekly chemo*
    - *Showed harm or increased side-effects from weekly chemo?*
  - *Which method do you think your patients prefer? If so, why?*
  - *Are there some methods used which aren't good? If so, why?*
  - *Did you look at the webpage? If so, what did you think of it?*
    - *Look through webpage now*
      - *Figures*
      - *Further info & support contacts*
      - *Video*
      - *FAQ*
  - *How could it be improved?*
  - *Did you look at the printed summary? What did you think of it?*
    - *Look through printed summary now*
    - *What do you think of the content of the results section?*
  - *This is the email your participants could sign up to receive. What do you think of it?*

If site was not randomised to printed summaries:

- Do you know if any of your participants had difficulty accessing the webpage or email list?
  - Did anyone ask you for a print out of the results?
  - Did anyone ask you to tell them the results?

- What do you think of the process of informing participants of the results – sending the update information sheets first?
  - *Is that enough preparation for participants?*

- *Do you think it is personal enough?*
- *Is the opt-out approach for the printed summaries a good one?*

Some other sites were randomised to communicate results to participants using [*email list / basic webpage / enhanced webpage / printed summaries sent by post*]. *Show webpage/printed summary / email and give time to look at. Highlight differences from other webpage.*

- What do you think of this/ these approaches to communicating the ICON8 results?
  - *Content*
  - *Method of delivery*
  - *Which bits you like / dislike*
- Would you like to have been offered any of these approaches as well as or instead of the approaches you were able to offer to participants?
  - *Why?*

Views on future practice

- How should the overall survival results of ICON8 be communicated to participants?
  - *Who should do it?*
  - *Which methods?*
  - *Which process?*
  - *To whom?*
    - *All patients*
    - *Relatives?*
  - *Why?*
  - *When?*

General recommendations

- What do you think should be done to communicate the results of other trials to participants?
  - *Who should do it?*
  - *Methods?*
  - *Process?*
  - *To whom?*
    - *All patients*
    - *Relatives?*
  - *When?*
  - *Why?*

- Are there any exceptions to this?
  - *Does it matter which arm participants were on, in cases where there is a difference in outcomes?*

- What advice would you give to people working at sites on other trials on how to share the results with participants?

- What advice would you give to people working at clinical trials units on other trials on how to share the results with participants?

- Is there anything else you'd like to say about this topic?

Thanks and wrap up

- Thank you
- This information will help us improve how we communicate results to trial participants
- We will share the overall results of this study with sites, when they are available.

Annex 6: Themes and high-level codes

These tables present the themes, sub-themes, and high-level codes, and how they relate to concepts from the Information Seeking and Communication Model[1], organised by the research question to which they relate.

[1] Robson A. Modelling information behaviour: linking information seeking and communication. Ph.D., The City University (London) (United Kingdom), Ann Arbor, 2013.

Table A6.1: What are the experiences and views of women in the ICON8 ovarian cancer trial on how the results were communicated to them?

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Patients' desire to receive trial results	Wanting to know the results	7.4.1	Demand for results	Information User's motivating factors
			Closure	
			Seeing if the trial was any use	
			We do trials to find out the results	
	Not wanting to know the results	7.4.2	Not wanting to think about cancer	Information non-use; Information User's inhibiting factors
Patients' experiences of receiving the ICON8 results	Patients' responses to receiving the Patient Update Information Sheet	7.6	Uncertainty about whether they received it	Communication process
			Actions on receiving the Patient Update Information Sheet	Outcomes
			Thoughts on receiving the Patient Update Information Sheet	
			Emotional responses to receiving the Patient Update Information Sheet	
	Reading and processing the results	7.7.1	Reading the results	Using communication
			Processing the results	
			Reading the results with others	

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Patients' experiences of receiving the ICON8 results	Finding out the results in other ways	7.7.2	Being told results by site staff	Information User's experience receiving the results
			Researching it for themselves	
	Outcomes of finding out the ICON8 results	7.8	Discussing the results with others	Outcomes
			Keeping the results	
			Sharing the results and their trial experiences with others	
Patient reactions to finding out the ICON8 results	Intellectual responses	7.9.1	The results are interesting	Outcomes
			The results are important	
			Patients' interpretations of the results and their implications	
			Raising questions	
	Emotional responses	7.9.2	Surprise	
			Positive emotional responses	
			Negative emotional responses	
			Mixed emotional responses	
			Reflections on the results and their randomised treatment allocation	

Table A6.2: What aspects of the mode of communication influence satisfaction with how the results are communicated, and why?

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Views of patients and site staff on the communication medium	Ease of access	5.2.8.2	Accessibility of posted printed summaries	Communication medium
			Not knowing how to access the results	Information User's experience receiving the results
			Accessibility of electronic approaches to sharing results	Communication medium
			Other ways in which patients found out the ICON8 results	
	Approaches based on a printed summary	8.2.1	Accessible to all	
			Good for sharing	
			Cost	
	Electronic means of communication	8.2.2	Access to computers / internet	
			Emails are quick and simple	
			Emails are more personal	
			Feasibility of emails	
	Personal approaches	8.2.3	Telephone calls	
			Face-to-face	
	Group meetings	8.2.4	Feasibility	
			Can clarify things	
			Not private	
	Giving participants choice	8.2.5	Need for different approach in different circumstances	
			Offer variety	

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Information	Understandability of the information	5.2.7.2	Easy to understand	Information
			Difficult to understand	
	Level and length of information	8.3.1	Short and simple	
			Too wordy	
	Language used	8.3.2	Clear and easy	
			Scientific terminology	
	Information items	8.3.3-12	Interesting and important information	
			Unnecessary information	
			Missing information	
			Information on survival	
			Diagrams	
			Links to further information and support	
			Frequently asked questions	
			Video	
			Thanks	
			Other information	

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Views on the Show RESPECT interventions	Layout and structure	8.4.1	Headings and broken-up text	Information product
			Use of columns	
			Use of colour	
			Structure	
			Navigation	
			Text size	
			Paper	
	Suggested adaptations	8.4.2	Adaptations to the webpages	
			Adaptations to the Printed Summary	
			Adaptations to the Email	
	Preferences between the interventions	8.4.3	Preferred webpage	
			Prefer Printed Summary	
Personalisation	(No) Need for personalisation	8.5	Need for personalisation	Communication process
			No need for personalisation	
	Personalising the interventions	8.5	Cover notes	
			Telephone calls	
Opt-in vs opt-out approaches	Opt-in approaches	8.6	Timing of opt-in	Communication process
			Feasibility of opt-in approaches	
	Opt-out approaches	8.6	Concerns with opt-out	
			Opt-out approaches are good	

Table A6.3: What other factors influence how satisfied women in the ICON8 trial were with how the results were communicated to them?

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Patients' motivation for joining the trial	Personal benefits	7.2.1	I could benefit	Information User's needs, wants, goals
	Altruism	7.2.2	Others could benefit	
Features that apply across all participants within a trial	Disease area and outcomes of interest	9.2.1	Prognosis of patients	Information
	Trial design, intervention(s) and control	9.2.2	Phase of trial	
			Placebo controlled trials	
			Trials in emergency settings	
	What the trial results show	9.2.3	(No) Need for different approach if there is a large difference	
			Easier to share 'good' news	

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Characteristics that vary between participants	Demographic factors	9.3.1	Age	Information User's context
			Education level	
			Frequency of internet and email use	
	Health factors	9.3.2	Randomised arm	
			Health at the time results are shared	
			Experience of side-effects during the trial	
	Relationship between site staff and participants	9.3.3.1	Close relationship	
			Not close relationship	
	Patients' understanding of potential trial outcomes	7.5, 9.3.3.2	Understanding potential trial outcomes	
			Understanding their prognosis	
			Lack of equipoise at time of joining trial	
	Patients' expectations around receiving results	7.3, 9.3.3.3	Expecting to receive results	
			Not expecting to receive results	
	Patients' reflections on being part of a trial	5.2.9.2	Cancer experience	
	Patients' access to support	9.3.3.4	Sources of support	

Table A6.4: What are the experiences and views of site staff in communicating the results of the ICON8 trial to the trial participants using the approaches tested in the Show RESPECT study?

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Site staff's access to and experience of sharing previous trial results	Site staff's access to study results	6.3.1	Access to study results	Provider's context
	Experience of sharing trial results with participants in other trials	6.3.2	Experience from other trials	
	Support from trials units to share results in other trials	6.3.3	Support from CTU	

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Site staff views on sharing results with trial participants	Motivation for sharing trial results with participants	6.4.1	Potential impact of the results for others	Provider's motivating factors
			Providing closure	
			Relating to the purpose of doing research	
	Site staff views on the benefits of sharing results with participants	6.4.2	Showing respect and valuating participants contributions	Provider's views
			Increasing awareness of the benefits of research	
			Helping participants process their trial experience	
	What inhibits site staff from sharing trial results with participants?	6.4.3	Concerns: depends on what's being communicated	Provider's inhibiting factors
			Concerns: emotional impact of the results	
			Concerns: none	
			Concerns: practicalities	
	Site staff perceptions of the views of colleagues	6.4.4	Views of colleagues	Provider's perceptions
	Responsibility for sharing results with participants	6.4.5	Should come from Sponsor	Provider's views
			Should come from site	
	Which trials should share results with participants?	6.4.6	Duty of candour	
			Sharing results – every trial	
			Sharing results – exceptions	
	Timing of sharing results	6.4.7	Timing of communicating results	Provider's views

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Site staff experience of sharing the ICON8 results	The process of sharing results	6.5.1	Preparing participants to receive the trial results	Communication process
			Checking participants' health	
			Finding addresses	
			Sending out the Patient Update Information Sheet	
			Leaving time between the stages of sharing results	
			Sending out Printed Summaries	
			Further follow-up and support	

Table A6.5: Which approaches to communicating the results of the ICON8 trial to participants are acceptable and feasible to implement for site staff and why?

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Concerns and challenges around sharing the ICON8 results	Concerns	6.4.3	Concerns: depends on what's being communicated	Provider's inhibiting factors
			Concerns: emotional impact of the results	
			Concerns: none	
			Concerns: practicalities	
	Challenges	6.5.2	Time	Communication process
			Working out who to send results to	
			Giving patients options	
			Patients not receiving posted documents	
			No challenges	
			Resource implications	

Table A6.6: Results that do not directly address any of the research questions

Theme	Sub-theme	Section	High-level codes	Information Seeking & Communication Model concept
Sharing results with others	Sharing results with participants in future trials	7.10.1	Advice for site staff	Communications process
			Advice for clinical trials units	
	Sharing results with families of participants	7.10.2	Reasons for sharing results with participants' families	Information User's motivating factors
			Who gets to decide whether participants' families should receive trial results?	n/a
			Practicalities of sharing results with families	Communications process
			Should we share results with families of participants who die during a trial?	n/a
			Experience of sharing results with families of participants who have died during a trial	Provider's context
			Who gets to decide whether we should share results with bereaved family members?	n/a
			Practicalities of sharing results with bereaved families	Communications process
	Sharing results with other patients	7.10.3	Sharing results with other patients	n/a
	Sharing results with GPs	7.10.4	Sharing results with GPs	n/a

Annex 7: Printed Summary

Participant summary
11 May 2018

MRC Clinical Trials Unit | UCL

Results of the ICON8 trial

ICON8

Thank you

Thank you for taking part in the ICON8 trial. You have helped us to answer important questions about how to treat women with ovarian cancer. We need you to carry on attending clinic visits so we can find out important longer term results. This will help other women with ovarian cancer in the future.

This document describes the results of the study, including statistics about survival and side effects. If you have any questions about the trial and its results, or if this summary raises any other worries for you, please speak to your oncologist or research nurse.

We wrote this summary in May 2018. We will have more results from this study at a later stage. This summary only includes results from the ICON8 trial. Other studies may find different results.

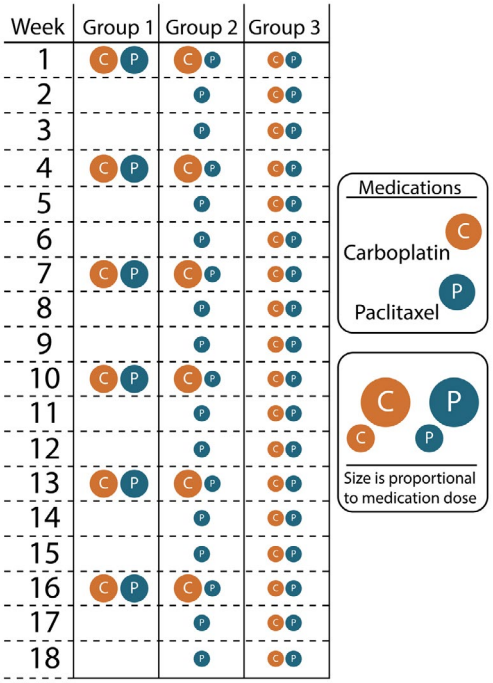
What was the ICON8 trial about?

The ICON8 trial tested how best to treat ovarian cancer. It compared three ways of giving chemotherapy:

- Standard chemotherapy, giving both carboplatin and paclitaxel (sometimes also called Taxol) once every three weeks for a total of 18 weeks (Group 1)
- Weekly chemotherapy, giving carboplatin once every three weeks and paclitaxel once a week (at a lower dose) for a total of 18 weeks (Group 2)
- Weekly chemotherapy, giving both carboplatin and paclitaxel once a week (at a lower dose) for a total of 18 weeks (Group 3)

The aim of the study was to see if having chemotherapy every week rather than every three weeks could:

- delay (or prevent) the cancer coming back or getting worse
- improve how long women with ovarian cancer lived (we hope to find out these results in 2019)



Why was the ICON8 trial needed?

Ovarian cancer is usually treated by a combination of surgery and chemotherapy. Surgery is done to remove as much of the cancer as possible. The initial chemotherapy used for ovarian cancer usually involves two drugs, carboplatin and paclitaxel (sometimes also called Taxol). Chemotherapy might be started before or after surgery, depending on the extent of cancer. These drugs are recommended by international experts for treating ovarian cancer. They are referred to as 'standard chemotherapy'. This treatment is usually given six times, once every three weeks over 18 weeks.

A previous study in Japan suggested that giving chemotherapy more often than once every three weeks may also be effective. This type of treatment involves giving paclitaxel and/or carboplatin at a lower dose every week for 18 weeks during treatment, rather than a larger dose once every three weeks. In this information sheet we call this 'weekly chemotherapy'.

In this study we wanted to find out if weekly chemotherapy is better than standard chemotherapy in treating women with ovarian cancer. We also wanted to see if weekly chemotherapy causes more or fewer side-effects than standard chemotherapy. Although weekly chemotherapy involves more doses of chemotherapy than standard chemotherapy, the treatment course is the same length for both.

Who took part in the ICON8 trial?

People taking part in the ICON8 trial were:

- female and at least 18 years old
- diagnosed with stage Ic, II, III or IV ovarian cancer, fallopian tube cancer or primary peritoneal cancer
- well enough to be up and about for at least half the day
- starting treatment for ovarian cancer for the first time

The trial took place in almost 100 UK hospitals as well as hospitals in Korea, the Republic of Ireland, Mexico, Australia and New Zealand.

1566 women took part in the ICON8 trial. The average age of women who joined ICON8 was 62, ranging from 22 to 84 years old. Most women had advanced ovarian cancer (stage IIIC or stage IV).

How was the ICON8 trial carried out?

Women joined the ICON8 trial between June 2011 and November 2014.

People who agreed to take part in the trial were put into three groups.

- Group 1 (522 women): received standard chemotherapy, having both carboplatin and paclitaxel once every three weeks for a total of 18 weeks.
- Group 2 (523 women): received weekly chemotherapy, having carboplatin once every three weeks and paclitaxel once a week (at a lower dose) for a total of 18 weeks
- Group 3 (521 women): received weekly chemotherapy having both carboplatin and paclitaxel once a week (at a lower dose) for a total of 18 weeks

Women in ICON8 could have surgery before or part way through their chemotherapy. Most women did have surgery.

So far, we have followed up how women were doing for at least 3 years. We wanted to see if having chemotherapy every week rather than every three weeks could delay (or prevent) the cancer coming back or getting worse, and improve how long women with ovarian cancer lived. We also looked at the side-effects women taking part in the study reported.

What did the ICON8 trial find?

The ICON8 trial found no difference in how long it was until the cancer came back or get worse for women who had weekly chemotherapy, compared to women who had three weekly chemotherapy.

On average, women who had chemotherapy every three weeks (Group 1) had around **24** months before their cancer came back or got worse. Women who had carboplatin every three weeks, and paclitaxel every week (Group 2) had around **25** months before their cancer came back or got worse, on average. Women who had carboplatin and paclitaxel every week (Group 3) also had around **25** months, on average, before their cancer came back or got worse. This difference is not big enough for us to be confident that having weekly chemotherapy is better than having chemotherapy once every three weeks. These results are averages. This means some women have done better, with the disease not coming back or getting worse, and others have had their disease come back or get worse sooner.

We found no evidence of any subgroups of women taking part in ICON8 benefitting from weekly chemotherapy compared to three-weekly chemotherapy. We looked at subgroups including stage of disease, and whether chemotherapy was started before or after surgery.

Many women in the study told us they had some side-effects. The main severe side-effects are shown in the graph.

The main side-effects were:

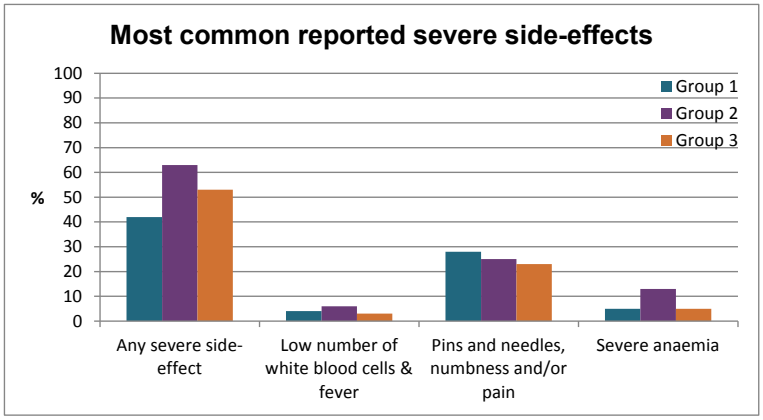
- Having a low number of white blood cells and a fever
- Pins and needles, numbness, and/or pain, usually in your feet
- Severe anaemia (low numbers of red blood cells, or low levels of haemoglobin in the blood)

The difference in numbers of women having any severe side-effect, a low number of white blood cells and a fever, or pins and needles numbness and /or pain is not big enough for us to be sure that it was due to the different treatment approaches. The difference in numbers who had severe anaemia is big enough for us to be confident that women in Group 2 were more likely to have severe anaemia than women in the other groups because of the treatment approach used in that group.

Women in Group 3 (who had weekly carboplatin) were more likely to have an allergic reaction to carboplatin than women who only had it once every three weeks (groups 1 and 2). These reactions were mostly mild.

Generally, women's quality of life improved during the trial. Women in Group 1 saw a faster improvement in quality of life than those in Group 2 or 3. But nine months after joining the trial, women's quality of life was similar in all three groups.

Weekly chemotherapy was safe to give, but did not work better than 3 weekly chemotherapy as



a first treatment for ovarian cancer. We think carboplatin and paclitaxel every 3 weeks should still be the standard treatment.

How sure can we be about these results?

The ICON8 trial had a large number of women taking part in it. This means we can be confident that having chemotherapy every week does not delay or prevent the cancer coming back or getting worse compared to having chemotherapy once every three weeks.

We do not currently know whether having chemotherapy once a week rather than once every three weeks improves how long women with ovarian cancer live for. We will need to follow-up women in ICON8 for longer to answer this question.

These results differ from an earlier trial in Japan, which showed that weekly chemotherapy increased how long women lived for compared to those who had chemotherapy every three weeks. This difference may be due to genetic differences between Japanese women and women from Europe and other places.

What do these results mean?

What do these results mean for you?

These results do not affect how you should be treated in the future.

Please continue to come to your appointments with your study doctor, so we can keep track of how well you are. This will help us to find out if there are any differences between the groups in the longer term, and see if it improves how long women with ovarian cancer live.

What do these results mean for other people?

These results suggest that women like those in ICON8 with ovarian cancer are unlikely to benefit from having chemotherapy once a week rather than once every three weeks.

ICON8 did not include women who were so unwell they were confined to bed for more than half of every day, so we do not know if they apply to them.

Evidence from the earlier Japanese trial suggests that Japanese women may benefit from weekly rather than three-weekly chemotherapy.

What difference will these results make?

These results will not change the way that future patients are treated. But they help doctors to understand more about how chemotherapy should be given to women with ovarian cancer. This may help them find other, better ways to treat ovarian cancer in the future.

The ICON8 trial will continue to follow-up women to answer the longer term question on whether weekly chemotherapy improves how long women live for.

A follow-on trial is now running called the ICON8B trial. ICON8B is looking at whether weekly chemotherapy is better than three-weekly chemotherapy for women who are also receiving the drug bevacizumab (also known as Avastin) in addition to chemotherapy.

Thank you

Once again, thank you for taking part in the ICON8 trial. You are helping us to answer important questions about how to treat women with ovarian cancer. We hope that the results of this trial will help women with ovarian cancer in the future.

Further information

If you have any questions about the ICON8 trial, please speak to your doctor or research nurse.

The ICON8 trial is registered with the ISRCTN registry. The registration number is 10356387. You can see more details about the trial here http://www.isrctn.com/ISRCTN10356387

The ICON8 trial was sponsored by the Medical Research Council. It was funded by Cancer Research UK.

Annex 8: Results Email

Results of the ICON8 trial

Thank you

Thank you for taking part in the ICON8 trial. You have helped us to answer important questions about how to treat women with ovarian cancer. We need you to carry on attending clinic visits so we can find out important longer term results. This will help other women with ovarian cancer in the future.

This email describes the results of the study, including statistics about survival and side effects. If you have any questions about the trial and its results, or if this summary raises any other worries for you, please speak to your oncologist or research nurse.

We wrote this summary in May 2018. We will have more results from this study at a later stage. This summary only includes results from the ICON8

What's in this email?

Clink on the links below to skip straight to a section.

trial. Other studies may find different results.

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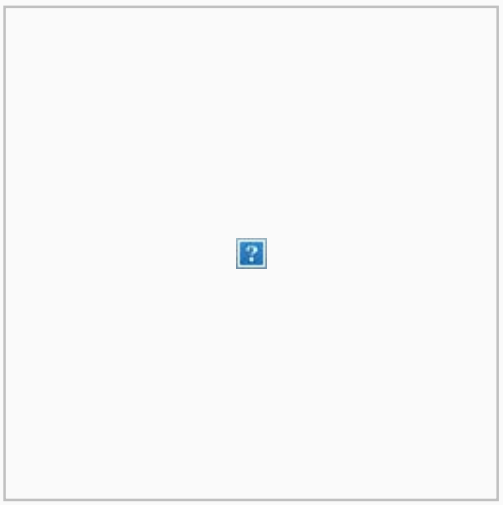

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A previous study in Japan suggested that giving chemotherapy more often than once every three weeks may also be effective. This type of treatment involves giving paclitaxel and/or carboplatin at a lower dose every week for 18 weeks during treatment, rather than a larger dose once every three weeks. We call this "weekly chemotherapy".

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We found no evidence of any subgroups of women taking part in ICON8 benefitting from weekly chemotherapy compared to three-weekly chemotherapy. We looked at subgroups including stage of disease, and whether chemotherapy was started before or after surgery.

Many women in the study told us they had some side-effects. The main side-effects were:

- Having a low number of white blood cells and a fever
- Pins and needles, numbness, and/or pain, usually in your feet
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The difference in numbers of women having any severe side-effect, a low number of white blood cells and a fever, or pins and needles numbness and /or pain is not big enough for us to be sure that it was due to the different treatment approaches. The

difference in numbers who had severe anaemia is big enough for us to be confident that women in Group 2 were more likely to have severe anaemia than women in the other groups because of the treatment approach used in that group.

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Generally, women's quality of life improved during the trial. Women in Group 1 saw a faster improvement in quality of life than those in Group 2 or 3. But nine months after joining the trial, women's quality of life was similar in all three groups.

Weekly chemotherapy was safe to give, but did not work better than 3 weekly chemotherapy as a first treatment for ovarian cancer. We think carboplatin and paclitaxel every 3 weeks should still be the standard treatment.

How sure can we be about these results?

The ICON8 trial had a large number of women taking part in it. This means we can be confident that having chemotherapy every week does not delay or prevent the cancer coming back or getting worse compared to having chemotherapy once every three weeks.

We do not currently know whether having chemotherapy once a week rather than once every three weeks improves how long women with ovarian cancer live for. We will need to follow-up women in ICON8 for longer to answer this question.

These results differ from an earlier trial in Japan, which showed that weekly chemotherapy increased how long women lived for compared to those who had chemotherapy every three weeks. This difference may be due to genetic differences between Japanese women and women from Europe and other places.

What do these results mean?

What do these results mean for you?

These results do not affect how you should be treated in the future.
Please continue to come to your appointments with your study doctor, so we can keep track of how well you are. This will help us to find out if there are any differences between the groups in the longer term, and see if it improves how long women with ovarian cancer live.

What do these results mean for other people?

These results suggest that women like those in ICON8 with ovarian cancer are unlikely to benefit from having chemotherapy once a week rather than once every three weeks.
ICON8 did not include women who were so unwell they were confined to bed for more than half of every day, so we do not know if they apply to them.
Evidence from the earlier Japanese trial suggests that Japanese women may benefit from weekly rather than three-weekly chemotherapy.

What difference will these results make?

These results will not change the way that future patients are treated. But they help doctors to understand more about how chemotherapy should be given to women with ovarian cancer. This may help them find other, better ways to treat ovarian cancer in the future.

The ICON8 trial will continue to follow-up women to answer the longer term question on whether weekly chemotherapy improves how long women live for.

A follow-on trial is now running called the ICON8B trial. ICON8B is looking at whether weekly chemotherapy is better than three-weekly chemotherapy for women who are also receiving the drug bevacizumab (also known as Avastin) in addition to chemotherapy.

Thank you

Once again, thank you for takin part in the ICON8 trial. You are helping us to answer important questions about how to treat women with ovarian cancer. We hope that the results of this trial will help women with ovarian cancer in the future.

Further information

If you have any questions about the ICON8 trial, please speak to your doctor or research nurse.

Cancer Research UK has information about ICON8 on their website

The ICON8 trial is registered with the ISRCTN registry. The registration number is 10356387

The ICON8 trial was sponsored by the Medical Research Council. It was funded by Cancer Research UK.

Target Ovarian Cancer have some useful information and support guides on their website, as do Ovacome and Cancer Research UK

Any questions?

Do you have a question about the ICON8 trial and what it found? Submit your question, and we will try to post an answer to it in the next email.

If you have a question about your own health or individual results, please ask your doctor or research nurse, who will be able to help you.

Support

Target Ovarian Cancer have a Support Line where you can speak to a nurse advisor. You can call the Support Line on 020 7923 5475.

Ovacome also have a Support Service that offers information and emotional support to women, their families, friends and carers. You can call the Support Service on 0800 008 7054, text them on 07427 390504, or instant message them on their website.

To find a Support Group or Service near you, visit Ovacome's list of local Support Services.

My Ovacome is an online community for anyone affected by ovarian cancer. It is a safe, supportive space for women with ovarian cancer and their friends and families to share their experiences and offer each other encouragement, knowledge, understanding and friendship.

Target Ovarian Cancer also has information about other sources of support on their website

Tell us what you think about this email

We are trying to improve how we communicate trial results to people taking part in our trials. If you have any comments about this email, please tell us.

Annex 9: Patient Update Information Sheet

Patient update
11 May 2018

MRC Clinical Trials Unit

UCL

ICON8

An international phase III randomised trial of dose-fractionated chemotherapy compared to standard three-weekly chemotherapy, following immediate primary surgery or as part of delayed primary surgery, for women with newly diagnosed epithelial ovarian, fallopian tube or primary peritoneal cancer

Introduction

We now have the first results from the ICON8 study. This information sheet contains details of what the next steps are for you and the study. It will also tell you how you can find out the results of the ICON8 study.

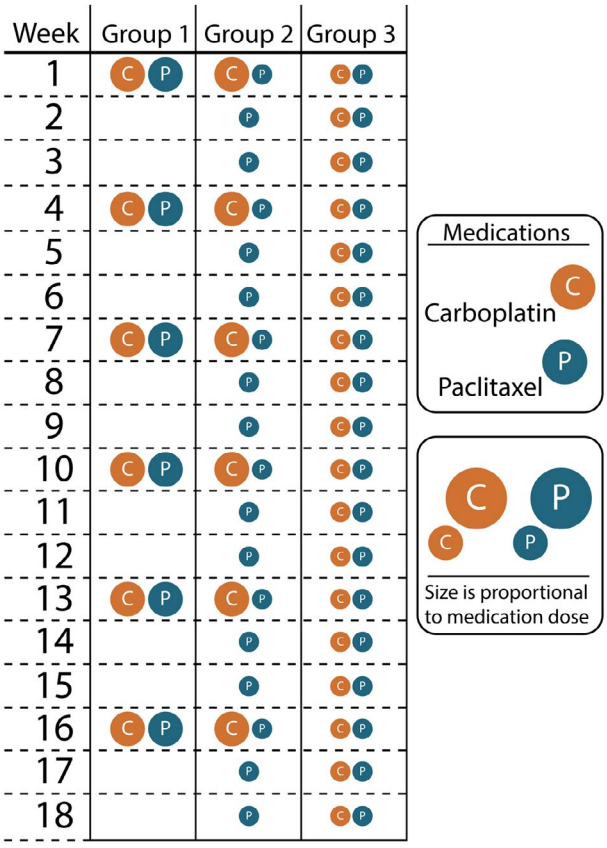
The ICON8 study is testing how best to give chemotherapy to women with ovarian cancer. It compared having chemotherapy every week to the current standard of having chemotherapy once every three weeks. It aimed to see if weekly chemotherapy is better at delaying or preventing the disease getting worse and improving how long women live for.

Women who agreed to take part in the ICON8 study were split into 3 groups, at random.

- 522 women were in group 1. They received standard chemotherapy, with two drugs (paclitaxel and carboplatin) given once every 3 weeks for 6 treatments (cycles). This took 18 weeks in total.
- 523 women were in group 2. They received the chemotherapy drug paclitaxel once a week, and the drug carboplatin once every 3 weeks for 6 cycles. This took 18 weeks in total.
- 521 women were in group 3. They received both paclitaxel and carboplatin once a week for 18 weeks.

Thank you

Thank you for taking part in the ICON8 study. You are helping us to answer important questions about how to treat women with ovarian cancer. This will help other women with ovarian cancer in the future.



Reference numbers

IRAS ID: 11/LO/0043
ISRCTN: 10356387

Annex 9

What is happening now in the ICON8 study?

All the women in ICON8 have completed their study treatment. We are now in the 'follow-up' phase. This is where we keep track of how you are doing, but your current and future treatment is the same as patients who are not in the trial.

Your study doctors and nurses will continue to monitor how you are, as part of the trial. This will help us to answer questions about the long-term effect of weekly chemotherapy.

How can I report side-effects?

When you see your doctor or research nurse at each hospital visit they will ask you about any side-effects you have had. It is important that you tell your doctor or research nurse about any problems. We will monitor you closely for any possible side-effects and your doctor or nurse may suggest extra tests if he/she considers it appropriate.

What results will be available and when?

We now have results telling us about whether weekly chemotherapy delays ovarian cancer getting worse, compared to having chemotherapy once every three weeks.

We do not yet know whether weekly chemotherapy makes a difference to how long women live, on average, compared to having chemotherapy once every three weeks. We expect these long-term results to be ready sometime in 2019.

How can I find out the results of the research?

We have put a summary of the results on this webpage [insert URL], which you can visit if you want to find out the results.

We will post you a written summary of the results. If you **do not** want us to send you the results, please tell your research nurse or doctor within the next three weeks. If we do not hear from you, we will assume that you would like the results to be posted to you.

If you want us to email you a summary of the results, sign-up for our email list here [insert URL of sign-up form]

Will I be given any results about me as an individual?

Your doctor has already discussed the results of any tests or scans you have had with you when they became available. If you have any questions about these, please ask your doctor or research nurse.

Which group of the study was I in?

If you would like to be reminded about which group of the study you were in, please ask your doctor or research nurse.

If I have any questions, whom should I contact?

If you have any questions about the ICON8 study, please speak to your doctor or research nurse.

Further information

ICON8 study is registered with the ISRCTN registry. The registration number is 10356387. You can see more details about the trial http://www.isrctn.com/ISRCTN10356387

The ICON8 study was sponsored by the Medical Research Council. It was funded by Cancer Research UK.