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Barriers to recruitment for surgical trials in head and neck oncology: a survey of trial investigators

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ABSTRACT

Objectives: Many randomised trials in surgery suffer from recruitment rates that lag behind projected targets. We aim to identify perceived barriers to recruitment among these pioneering trials in the field of head and neck cancer surgery.

Design: Recruiting centres to all three trials (Selective Elective Neck Dissection (SEND), Positron Emission Tomography (PET)-Neck and Hyperbaric Oxygen in the Prevention of Osteoradionecrosis (HOPON)) were contacted by email by the chief investigators. Responders were asked to complete a web-based survey in order to identify the barriers to recruitment in their centre and grade each by severity.

Setting: Secondary care: 44 head and neck oncology regional referral centres.

Participants: Analysis was based on 85 responses evenly distributed between the three trials.

Results: The most commonly identified perceived barriers to recruitment (more than 50% of responders identified the item as a barrier in all the three trials) in the order of frequency were: patients consent refusal because of expressed treatment preference, patients consent refusal owing to aversion to randomisation, excess complexity/ amount of information provided to patients and lack of time in clinic to accommodate research. The most severely rated of these problems was consent refusal because of the expressed treatment preference and lack of time in the clinic.

Conclusions: Our findings confirm others' work in surgery that the most significant barrier to trial recruitment in head and neck cancer surgery is the patient's preference for one arm of the trial. It may be that additional training for those taking consent may be helpful in this regard. It is also important to adequately resource busy surgical clinics to support clinical trial recruitment.

INTRODUCTION

The requirement to formally evaluate new innovations and re-evaluate established treatments of doubtful value demands evidence from randomised controlled trials (RCTs).[1] At 16 years after the *Lancet* highlighted this issue in 'Surgical research or comic opera',[2] the paucity of trials remains a major issue for

surgery.[3] Problems with timely recruitment seen in many RCTs also appear to be concentrated in surgical trials. A review of all RCTs funded by the Medical Research Council (MRC) and National Commissioning Centres Health Technology Assessment (HTA) Unit between 1994 and 2002 found that only 31% of these trials recruited to their original target.[4] Recent UK data confirm trial recruitment problems in surgery, with only 25% of the 60 current studies recruiting at better than 80% of target (Gower J, personal correspondence, National Institute of Health Research (NIHR) data, 2012). Recruitment to randomised trials of surgical interventions is challenging because of several factors

including the complexity of surgery and perhaps even the nature of surgeons.[5] It is thought that surgeons are less tolerant of uncertainty or having their practice scrutinised externally. Recently, a National Institute of Health Research (NIHR) Working Party addressing this problem has been formed: Growing Recruitment in Interventional and Surgical Trials (GRIST).[1] GRIST aims to enhance recruitment to interventional trials, identify restricting factors in 'trials clinics', develop pilot studies of recruitment and improve the identification of eligible patients. It also aims to increase the number of interventional and surgical studies within the NIHR portfolios.

In oncology, it has been estimated that at least half of the curative impact of treatment can be attributed to surgery; however, surgical studies receive only 2.8% of UK cancer funding (source of data: Cancer Research UK 2012). The majority of patients with cancer are receptive to RCT participation,[6] but it has been found that enthusiasm to recruit is stronger among medical than surgical oncologists.[7] In one discrete area of surgical oncology, head and neck (H&N) cancer, the first trials within the NIHR portfolio have recently opened. As there is little tradition in the UK for involving surgeons in randomisation of H&N patients with cancer, these new trials may highlight the generic barriers to recruitment for research-naive surgeons. Following discussion of H&N surgery trials progress at a GRIST 'trials clinic', it was decided to conduct a comprehensive survey of barriers to recruitment.

We report on a recruitment survey for the first three surgical phases, three RCTs in H&N oncology in the NIHR portfolio. SEND (Selective Elective Neck Dissection) is a Cancer Research UK funded trial measuring the benefit of selective neck dissection versus active monitoring in early stage oral cancer. The Positron Emission Tomography (PET)-Neck trial is an NIHR HTA funded trial that compares the efficacy of a PET-Computerised Tomography (CT) guided watch and wait policy with the current practice of planned neck dissection following chemotherapy/radiotherapy; the management of advanced regional metastasis for H&N squamous carcinoma. HOPON (Hyperbaric Oxygen in the Prevention of Osteoradionecrosis) is a Cancer Research UK funded trial that evaluates the ability of hyperbaric oxygen treatment to prevent osteoradionecrosis in previously irradiated H&N patients with cancer who need to undergo further surgery. These trials were open and actively recruiting patients at the time of conducting the survey, but recruitment was below the originally projected trajectory in all three.

The aims of this study are to identify general and trial-specific problems encountered in recruiting patients to SEND, PET-Neck and HOPON, evaluating the differences attributable to trial design, centre type and investigator background. This is the first study to explore the clinical teams' perspective with regard to the barriers to recruitment in H&N surgery trials. Attempting this analysis, it is emphasised that the underlying barriers to recruitment may be difficult to accurately determine from a survey as they will be subject to subjective interpretations by investigators. The findings will nevertheless inform the current debate around surgical trials, and indeed the attitude of surgical teams towards these trials. It is hoped that these data will form the basis of interventions to improve recruitment in these and other surgical trials.

METHOD

A web-based survey aimed that those recruiting and randomising to the three trials was developed using the online software SurveyGizmo. The list of barriers to recruitment was based on a modification of our recruitment survey tool[8] developed through previous publications in this area. Three surveys were constructed with a majority of identical common questions; however, additional trial-specific questions were added, for example, where excess treatment costs or availability of a specific trial investigation or treatment were a factor. The three trial management teams gave feedback on the presentation and content of the survey prior to its launch. Responders were asked to rate the barriers to recruitment on a scale, reporting the problems as either 0=no problem, 1=mild problem, 2=moderate problem or 3=severe problem. Participant nomination of additional factors and free text responses were invited in each section. Skip logic was applied and the questions were directed selectively to responders based on their responses to earlier questions. The barriers were classified as trial level, site level, patient-related and clinical team-related and information-related and consent-related factors (see online supplementary table S1).

The sampling frame was the clinical staff at all sites that had either recruited successfully or attempted to recruit to the trials. The mailing lists were compiled by the trial coordinators of the three trials and the link to the online survey, accompanied by a covering e-mail outlining the aims of the study, was sent out to sites. The clinical staff then forwarded the link to other staff members involved with trial recruitment, with staff involved in more than one trial requested to complete a separate questionnaire for each trial. Participation was voluntary and no personal information was collected. Individuals were contacted by two subsequent e-mail reminders spaced 2 weeks apart.

The primary aim of the study was to describe the perceived barriers to recruitment within and across the three trials. Partial responses were included in analyses if more than 25% of the questions had been answered. The most commonly identified barriers were defined as those where more than 50% of responders had identified a barrier as mild, moderate or severe problem in all the three trials. The barriers identified as mild, moderate or severe problem in any two of the trials were also highlighted. Secondary, exploratory analyses were undertaken to investigate the effect of trial, hospital type (teaching or district general hospital (DGH)) and responder role type (grouped as doctor or research

nurse but excluding 'other' types owing to limited numbers and heterogeneity of role types within this category) using ordinal logistic regression (adjusted for trial in analyses of hospital type and role type).

RESULTS

A total of 155 responses to the survey were received. However, 70 of these were partial responses (HOPON (14), PET-Neck (41) and SEND (15)) for which less than 25% of the questions were answered. The questionnaires were forwarded to all trial contacts via the three trial management teams in order to retain confidentiality of investigators. It was felt that the largely incomplete surveys had been opened by individuals connected with the trial but not involved in randomising patients. Accordingly, these were excluded from all analyses as they did not provide any useable data. Analyses are based on 85 responses, similarly distributed across trials (table 1), with a modest amount of missing data.

Responders were from a total of 44 UK recruiting sites with 11 sites contributing to more than one of the HOPON, PET-Neck and SEND surveys. The percentage of sites from each trial that responded to the survey varied between 50% (HOPON), 40% (PET-Neck) and 53% (SEND). Approximately 40% of the responses in each trial were from site principal investigators with some variation across studies in other responder role types (table 1). The percentage of responding sites that were teaching hospitals was similar for HOPON (60%)

and SEND (63%) with a much lower percentage for the PET-Neck (26%) trial. The number of responses according to severity, presented by trial type, hospital type (teaching versus DGH) and by occupation of responder (medical practitioner and research nurse) are displayed for each trial-specific (table 2), site-specific (table 3), patient-specific (table 4), clinical team-specific (table 5) and patient information-specific and consent-specific problem (table 6).

The most commonly identified perceived barriers to recruitment (more than 50% of responders identified the item as a barrier in all three trials), in the order of frequency were: patients consent refusal because of expressed treatment preference, patients consent refusal owing to aversion to randomisation, excess complexity/amount of information provided to patients and lack of time in clinic to accommodate research. The most severely rated of these problems were the consent refusal because of expressed treatment preference and lack of time in the clinic.

Commonly identified barriers in two of the three trials also highlighted: incompatibility with trial protocol, educational/socioeconomic level of patients, lack of research experience in the clinical team, inadequate time for trial administration and consultant/surgeon's preference for one arm of the trial. The most severely rated of these problems was the incompatibility of study protocol with clinical practice.

Although the differences between the trials were not as important as the common themes, some areas were commonly highlighted in specific trials. Ordinal logistic

Table 1 Characteristics of survey responders and sites

	HOPON	PET-Neck	SEND
Number of responders	27	31	27
Number of sites that responded/number of sites invited (%)	20/40 (50)	21/52 (40)	16/30 (53)
Number of responders per site, median (range)	1 (1,4)	1 (1,3)	1.5 (1,4)
Role of responder, n (%)			
Site principal investigator	11 (41)	12 (39)	11 (41)
Other investigator	6 (22)	1 (3)	8 (30)
Research nurse/practitioner	3 (11)	13 (42)	6 (22)
Others	7 (26)	5 (16)	2 (7)
Region*, n (%)			
North	6 (22)	12 (39)	8 (30)
Midlands	3 (11)	3 (10)	9 (33)
Southwest	6 (22)	7 (23)	1 (4)
Wales	–	1 (3)	–
Scotland	4 (15)	4 (13)	1 (4)
International	2 (7)	–	–
London	4 (15)	0 (0)	1 (4)
East	–	–	0 (0)
Northern Ireland	–	0 (0)	–
Home counties	2 (7)	4 (13)	7 (26)
Type of setting, n (%)			
Teaching	16 (59)	8 (26)	17 (63)
DGH	11 (41)	23 (74)	10 (37)

*Hospitals were grouped according to recruitment site.
DGH, district general hospital; HOPON, Hyperbaric Oxygen in the Prevention of Osteoradionecrosis; SEND, Selective Elective Neck Dissection.

Table 2 Trial-specific problems

Potential problems	Severity of problem	Trial			Hospital type		Role type	
		HOPON (n=27)	PET-Neck (n=31)	SEND (n=27†)	DGH (n=44)	Teaching hospital (n=41†)	Medical practitioners (n=49†)	Research nurses (n=22)
Complexity of trial design	No problem	18 (67)	17 (55)	18 (67)	28 (64)	25 (61)	30 (61)	15 (68)
	Mild	7 (26)	10 (32)	7 (26)	12 (27)	12 (29)	16 (33)	4 (18)
	Moderate	2 (7)	4 (13)	2 (7)	4 (9)	4 (10)	3 (6)	3 (14)
	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	p Value*	0.52			0.52		0.41	
Problems with day to day communication with trial team	No problem	22 (81)	22 (71)	20 (77)	31 (70)	33 (83)	35 (73)	18 (82)
	Mild	5 (19)	7 (23)	5 (19)	12 (27)	5 (13)	12 (25)	3 (14)
	Moderate	0 (0)	1 (3)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)
	Severe	0 (0)	1 (3)	1 (4)	1 (2)	1 (3)	1 (2)	1 (5)
	p Value*	0.59			0.35		0.27	
Problems with explanation of trial at set-up meeting	No problem	20 (74)	21 (68)	18 (69)	32 (73)	27 (68)	30 (63)	19 (86)
	Mild	7 (26)	9 (29)	4 (15)	10 (23)	10 (25)	13 (27)	3 (14)
	Moderate	0 (0)	1 (3)	2 (8)	2 (5)	1 (3)	3 (6)	0 (0)
	Severe	0 (0)	0 (0)	2 (8)	0 (0)	2 (5)	2 (4)	0 (0)
	P Value*	0.75			0.48		0.02	
Inclusion/exclusion criteria too stringent	No problem	20 (74)	21 (68)	14 (54)	28 (64)	27 (68)	29 (60)	16 (73)
	Mild	4 (15)	10 (32)	10 (38)	13 (30)	11 (28)	17 (35)	4 (18)
	Moderate	3 (11)	0 (0)	2 (8)	3 (7)	2 (5)	2 (4)	2 (9)
	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	p Value*	0.34			0.53		0.48	
Incompatibility of study protocol with clinical practice	No problem	14 (52)	12 (39)	6 (23)	20 (45)	12 (30)	16 (33)	10 (45)
	Mild	8 (30)	10 (32)	4 (15)	11 (25)	11 (28)	11 (23)	4 (18)
	Moderate	5 (19)	5 (16)	12 (46)	8 (18)	14 (35)	16 (33)	5 (23)
	Severe	0 (0)	4 (13)	4 (15)	5 (11)	3 (8)	5 (10)	3 (14)
	p Value*	0.01			0.28		0.33	
Competing trials for the same patients	No problem	24 (89)	29 (94)	24 (89)	41 (93)	36 (88)	43 (88)	22 (100)
	Mild	3 (11)	1 (3)	3 (11)	2 (5)	5 (12)	5 (10)	0 (0)
	Moderate	0 (0)	1 (3)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)
	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	p Value*	0.81			0.54		0.95	

*p Value from ordinal logistic regression model (adjusted for trial in hospital type and role type analyses).
†One missing response for some items.
DGH, district general hospital; HOPON, Hyperbaric Oxygen in the Prevention of Osteoradionecrosis; SEND, Selective Elective Neck Dissection.

Table 3 Site-specific problems

Potential problems	Severity of problem	Trial			Hospital type		Role type	
		HOPON (n=27)	PET-Neck (n=31)	SEND (n=27†)	DGH (n=44)	Teaching hospital (n=41†)	Medical practitioners (n=49†)	Research nurses (n=22)
R&D delays	No problem	18 (67)	18 (58)	21 (81)	26 (59)	31 (78)	28 (58)	15 (68)
	Mild	7 (26)	8 (26)	4 (15)	12 (27)	7 (18)	12 (25)	7 (32)
	Moderate	2 (7)	3 (10)	0 (0)	3 (7)	2 (5)	5 (10)	0 (0)
	Severe	0 (0)	2 (6)	1 (4)	3 (7)	0 (0)	3 (6)	0 (0)
	p Value*	0.16			0.17		0.07	
Delays in local approval by Trust Research Board	No problem	19 (70)	24 (77)	20 (77)	32 (73)	31 (78)	29 (60)	20 (91)
	Mild	4 (15)	4 (13)	4 (15)	4 (9)	8 (20)	11 (23)	1 (5)
	Moderate	3 (11)	2 (6)	2 (8)	6 (14)	1 (3)	6 (13)	1 (5)
	Severe	1 (4)	1 (3)	0 (0)	2 (5)	0 (0)	2 (4)	0 (0)
	p Value*	0.75			0.29		0.02	
Research nurse/practitioner not available	No problem	12 (44)	21 (68)	18 (69)	27 (61)	24 (60)	25 (52)	16 (73)
	Mild	9 (33)	6 (19)	1 (4)	11 (25)	5 (13)	10 (21)	3 (14)
	Moderate	2 (7)	4 (13)	1 (4)	2 (5)	5 (13)	5 (10)	1 (5)
	Severe	4 (15)	0 (0)	6 (23)	4 (9)	6 (15)	8 (17)	2 (9)
	p Value*	0.23			0.95		0.26	
Problems with availability of required technology†	No problem	21 (78)	16 (52)	NA§				
	Mild	3 (11)	12 (39)					
	Moderate	1 (4)	2 (6)					
	Severe	2 (7)	1 (3)					
	p Value*	NA§			NA§		NA§	
Problems with funding for required technology‡	No problem	15 (55)	19 (61)	NA§				
	Mild	4 (15)	6 (19)					
	Moderate	1 (4)	4 (13)					
	Severe	7 (26	2 (6)					
	P Value*	NA§			NA§		NA§	
Lack of places on a GCP course locally	No problem	20 (74)	26 (84)	22 (85)	34 (77)	34 (85)	38 (79)	18 (82)
	Mild	6 (22)	5 (16)	3 (12)	10 (23)	4 (10)	8 (17)	4 (18)
	Moderate	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Severe	0 (0)	0 (0)	1 (4)	0 (0)	2 (5)	2 (4)	0 (0)
	p Value*	0.54			0.33		0.98	

*p Value from ordinal logistic regression model (adjusted for trial in hospital type and role type analyses).
†One missing response.
‡Hyperbaric oxygen, PET imaging or ARSAC licence (trial specific question).
§NA as question excluded from SEND trial as not relevant.
DGH, district general hospital; GCP course, Good Clinical Practice course; HOPON, Hyperbaric Oxygen in the Prevention of Osteoradionecrosis; R&D delays, research and development delays; SEND, Selective Elective Neck Dissection.

Table 4 Patient-specific problems

Potential problems	Severity of problem	Trial			Hospital type		Role type	
		HOPON (n=27†)	PET-Neck (n=31)	SEND (n=27‡)	DGH (n=44§)	Teaching hospital (n=41¶)	Medical practitioners (n=49¶)	Research nurses (n=22**)
Consent refusal because of expressed treatment	No problem	7 (31)	9 (29)	2 (8)	10 (24)	8 (21)	5 (11)	6 (29)
	Mild	6 (26)	13 (42)	6 (23)	16 (39)	9 (23)	16 (34)	7 (33)
	Moderate	9 (39)	4 (13)	14 (54)	11 (27)	16 (41)	20 (43)	5 (24)
	Severe	1 (4)	5 (16)	4 (15)	4 (10)	6 (15)	6 (13)	3 (14)
	p Value*	0.03			0.35		0.17	
Consent refusal because of aversion to randomisation	No problem	9 (39)	15 (48)	3 (12)	18 (44)	9 (23)	9 (19)	12 (57)
	Mild	9 (39)	12 (39)	10 (38)	14 (34)	17 (44)	21 (45)	6 (29)
	Moderate	5 (22)	3 (10)	11 (42)	8 (20)	11 (28)	14 (30)	3 (14)
	Severe	0 (0)	1 (3)	2 (8)	1 (2)	2 (5)	3 (6)	0 (0)
	p Value*	0.002			0.28		0.003	
Concerns about safety of either of trial treatments	No problem	13 (56)	22 (71)	13 (50)	27 (66)	21 (54)	24 (51)	17 (81)
	Mild	8 (35)	8 (26)	9 (35)	11 (27)	14 (36)	19 (40)	3 (14)
	Moderate	2 (9)	1 (3)	4 (15)	3 (7)	4 (10)	4 (9)	1 (5)
	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	p Value*	0.19			0.59		0.04	
Additional trial demands such as travelling and extra appointments	No problem	6 (26)	18 (58)	16 (64)	18 (44)	22 (58)	19 (41)	13 (62)
	Mild	7 (31)	10 (32)	7 (28)	14 (34)	10 (26)	18 (39)	5 (24)
	Moderate	6 (26)	2 (6)	2 (8)	7 (17)	3 (8)	6 (13)	2 (10)
	Severe	4 (17)	1 (3)	0 (0)	2 (5)	3 (8)	3 (7)	1 (5)
	p Value*	0.002			0.02		0.54	
Additional financial costs to the patient because of the trial	No problem	13 (57)	22 (71)	18 (72)	26 (63)	27 (71)	29 (63)	15 (71)
	Mild	7 (30)	7 (23)	5 (20)	12 (29)	7 (18)	12 (26)	5 (24)
	Moderate	2 (9)	2 (6)	2 (8)	3 (7)	3 (8)	4 (9)	1 (5)
	Severe	1 (4)	0 (0)	0 (0)	0 (0)	1 (3)	1 (2)	0 (0)
	p Value*	0.41			0.4		0.63	
Language or cultural barrier	No problem	18 (78)	25 (81)	22 (85)	35 (85)	30 (77)	35 (74)	20 (95)
	Mild	5 (22)	6 (19)	3 (12)	6 (15)	8 (21)	12 (26)	0 (0)
	Moderate	0 (0)	0 (0)	1 (4)	0 (0)	1 (3)	0 (0)	1 (5)
	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	p Value*	0.88			0.28		0.07	

*p Value from ordinal logistic regression model (adjusted for trial in hospital type and role type analyses).
†Four missing responses.
‡One or two missing responses.
§Three missing responses.
¶Two or three missing responses.
**One missing response.
DGH, district general hospital; HOPON, Hyperbaric Oxygen in the Prevention of Osteoradionecrosis; SEND, Selective Elective Neck Dissection.

Table 5 Clinical team problems

Potential problems	Severity of problem	Trial			Hospital type		Role type	
		HOPON (n=27)	PET-Neck (n=31)	SEND (n=27†)	DGH (n=44‡)	Teaching hospital (n=41‡)	Medical practitioners (n=49‡)	Research nurses (n=22‡)
Inadequate time to complete administration around the trial	No problem	13 (48)	20 (65)	11 (44)	28 (65)	16 (40)	17 (35)	17 (81)
	Mild	8 (30)	8 (26)	10 (40)	12 (28)	14 (35)	22 (46)	2 (10)
	Moderate	3 (11)	2 (6)	3 (12)	3 (7)	5 (13)	6 (13)	2 (10)
	Severe	3 (11)	1 (3)	1 (4)	0 (0)	5 (13)	3 (6)	0 (0)
	p Value*	0.24			0.03		0.005	
Lack of time in clinic to accommodate research	No problem	11 (41)	12 (39)	13 (50)	21 (49)	15 (37)	12 (24)	15 (71)
	Mild	7 (26)	10 (32)	3 (11.5)	8 (19)	12 (29)	15 (31)	2 (10)
	Moderate	8 (30)	5 (16)	7 (27)	11 (26)	9 (22)	14 (29)	4 (19)
	Severe	1 (4)	4 (13)	3 (11.5)	3 (7)	5 (12)	8 (16)	0 (0)
	p Value*	0.97			0.28		0.0005	
Lack of research experience in clinical team	No problem	11 (41)	22 (71)	13 (48)	28 (64)	18 (44)	21 (43)	17 (77)
	Mild	9 (33)	7 (23)	10 (37)	10 (23)	16 (39)	19 (39)	4 (18)
	Moderate	7 (26)	2 (6)	4 (15)	6 (14)	7 (17)	9 (18)	1 (5)
	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	p Value*	0.04			0.37		0.03	
Clinical team does not regard clinical research as important	No problem	20 (74)	28 (90)	17 (65)	40 (93)	25 (61)	34 (69)	19 (90)
	Mild	2 (7)	1 (3)	8 (31)	0 (0)	11 (27)	10 (20)	1 (5)
	Moderate	4 (15)	2 (7)	1 (4)	3 (7)	4 (10)	4 (8)	1 (5)
	Severe	1 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)
	p Value*	.0.13			0.009		0.22	
Clinical team does not regard the research question as important	No problem	23 (85)	22 (71)	14 (54)	36 (84)	23 (56)	28 (57)	19 (90)
	Mild	2 (7)	8 (26)	9 (35)	5 (12)	14 (34)	16 (33)	1 (5)
	Moderate	1 (4)	1 (3)	3 (11)	2 (5)	3 (7)	4 (8)	1 (5)
	Severe	1 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)
	p Value*	0.06			0.01		0.01	
Hesitation in involving oncology patients in randomised trials	No problem	23 (85)	26 (84)	17 (65)	38 (88)	28 (68)	37 (76)	17 (81)
	Mild	3 (11)	5 (16)	5 (19)	4 (9)	9 (22)	9 (18)	2 (10)
	Moderate	1 (4)	0 (0)	4 (15)	1 (2)	4 (10)	3 (6)	2 (10)
	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	p Value*	0.1			0.06		0.98	
Consultant/surgeon's preference for one arm of the trial	No problem	18 (67)	14 (45)	7 (27)	19 (44)	20 (49)	17 (35)	11 (52)
	Mild	7 (26)	9 (29)	11 (42)	13 (30)	14 (34)	19 (39)	6 (29)
	Moderate	1 (4)	6 (19)	5 (19)	7 (16)	5 (12)	11 (22)	1 (5)
	Severe	1 (4)	2 (7)	3 (12)	4 (9)	2 (5)	2 (4)	3 (14)
	p Value*	0.01			0.45		0.07	

*p Value from ordinal logistic regression model (adjusted for trial in hospital type and role type analyses).
†Two or three missing responses for some items.
‡One missing response for some items.
DGH, district general hospital; HOPON, Hyperbaric Oxygen in the Prevention of Osteoradionecrosis; SEND, Selective Elective Neck Dissection.

regression analyses including trial as a predictor variable suggest that SEND was significantly more likely to have more severe problems with incompatibility of study protocol with clinical practice (p=0.01), consent refusal because of expressed treatment preference (p=0.03) or aversion to randomisation (p=0.002) and consultant/surgeon's preference for one arm of the trial (p=0.01).

HOPON was significantly more likely to have more severe problems with additional trial demands of travelling and extra appointments (p=0.002).

After adjusting for trial, DGHs were significantly more likely to report the additional trial demands such as travelling and extra appointments as a higher severity grade of problem than teaching hospitals (p=0.02). On the other

Table 6 Patient information and consent-related problems

Potential problems	Severity of problem	Trial			Hospital type		Role type	
		HOPON (n=27†)	PET-Neck (n=31)	SEND (n=27†)	DGH (n=44†)	Teaching hospital (n=41†)	Medical practitioners (n=49†)	Research nurses (n=22)
Excess complexity/ amount of information provided to patients	No problem	10 (38)	13 (42)	8 (30)	15 (35)	16 (39)	12 (24)	12 (55)
	Mild	13 (50)	14 (45)	11 (41)	20 (47)	18 (44)	26 (53)	8 (36)
	Moderate	2 (8)	4 (13)	8 (30)	8 (19)	6 (15)	10 (20)	2 (9)
	Severe	1 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)
	p Value*	0.28			0.46		0.02	
Lack of training of person seeking consent	No problem	19 (73)	28 (90)	19 (73)	39 (91)	27 (68)	36 (75)	20 (91)
	Mild	4 (15)	2 (6)	3 (12)	2 (5)	7 (18)	7 (15)	1 (5)
	Moderate	2 (8)	1 (3)	4 (15)	2 (5)	5 (13)	4 (8)	1 (5)
	Severe	1 (4)	0 (0)	0 (0)	0 (0)	1 (3)	1 (2)	0 (0)
	p Value*	0.19			0.05		0.29	
Education level/ socioeconomic status of patients	No problem	14 (54)	15 (48)	9 (33)	22 (51)	16 (39)	16 (33)	13 (59)
	Mild	9 (35)	11 (35)	10 (37)	12 (28)	18 (44)	20 (41)	6 (27)
	Moderate	2 (8)	5 (16)	7 (26)	9 (21)	5 (12)	13 (27)	1 (5)
	Severe	1 (4)	0 (0)	1 (4)	0 (0)	2 (5)	0 (0)	2 (9)
	p Value*	0.17			0.61		0.04	

*p Value from ordinal logistic regression model (adjusted for trial in hospital type and role type analyses).
†One missing response for some items.
DGH, district general hospital; HOPON, Hyperbaric Oxygen in the Prevention of Osteoradionecrosis; SEND, Selective Elective Neck Dissection.

hand, teaching hospitals, perhaps surprisingly, were significantly more likely to identify a higher severity of problem with regard to inadequate time to complete administration around the trial (p=0.03), clinical team does not regard clinical research (p=0.009), or the research question (p=0.01), to be important.

Despite a reduced sample size (n=71) owing to excluding of the heterogeneous group of 'other' responder roles, the ordinal logistic regression analyses (adjusted for trial) suggest that medical practitioners were significantly more likely to report a higher grade of severity for problems with explanation of trial at set up meeting (p=0.02), delays in local approval by Trust research board (p=0.02), consent refusal owing to aversion to randomisation (p=0.003), concerns about safety of trial treatments (p=0.04), inadequate time to complete administration around the trial (p=0.005), lack of time in clinic to accommodate research (p=0.0005), lack of research experience in clinical team (p=0.03), clinical team does not regard research question as important (p=0.01), excess complexity/amount of information to patients (p=0.02) and education level/socioeconomic status of patients (p=0.04). Results from ordinal logistic regression analyses are exploratory and should be interpreted with caution as multiple statistical tests have been performed which increases the type I error rate.

DISCUSSION
This study explored barriers to recruitment in three NIHR portfolio RCTs led by, and largely recruited to by, surgeons in a clinical field not previously engaged in RCTs. These are the first surgical trials within the National Cancer Research Institute (NCRI) H&N portfolio, all of which have recruited below original planned rates. Although there were some minor differences between trials, the perceived barriers that appeared to present the most severe problems across the trials overall were that patients refused consent because of treatment preferences or were averse to randomisation, and that there is often insufficient time available in National Health Service (NHS) clinics to perform these portfolio trials. It was also felt that some of the patient information was too complex and did not reflect the socioeconomic profile or language skills of many patients affected by Head and Neck Squamous Cell Carcinoma (HNSCC).

A good response was received, reasonably evenly distributed from the three trials. As the responses were anonymised, it was not possible to link the data presented here with actual trial recruitment data. The few partial responses with <25% of questions completed were excluded and it was likely that these questionnaires were quickly abandoned by trials contacts not actually involved in recruiting patients and that discarding these data are not a significant detriment to the study. It was possible that more than one response was obtained per recruiting centre, and that some respondents involved in more than one trial gave responses to each trial questionnaire they received.

The most severe barriers to RCT recruitment shown here were patients' refusals to consent because of

treatment preference or because of aversion to randomisation. It is known that the lack of equipoise can be inadvertently relayed to patients by medical practitioners.[9] This results in poor trial recruitment; in work such as ours, is likely (and incorrectly) attributed to patient refusal to enter trials rather than clinician bias. Patient preference is rather complex and perhaps more dynamic than had been assumed, and may be a useful step in the consent process rather than an insurmountable barrier to recruitment.[10] Differences between patients' and surgeons' explanations for non-recruitment have also been highlighted in a recent meta-analysis including 23 surgical RCTs.[11] In this meta-analysis, it was found that patients' distrust of clinicians, aversion to randomisation or placebo arms and difficulty making decisions were frequently reported (by patients) in real RCTs. However, surgeon-reported factors emphasised these less, instead reported difficulties with informed consent, protocol complexity and also flagged the lack of incentives for surgeons to recruit to RCTs.

Qualitative analysis of recruitment consultations have found that clinicians often have bias in their explanation, and also their recall of their own explanation is significantly flawed.[12] By subsequently implementing improvements using more consistent messages, feedback and training, screen to randomisation rates have been transformed, for example, from 30% to 65% in the ProtecT RCT investigating the treatment of localised prostate cancer.[12] In our data, it is of course impossible to unravel the proportion of the barriers to recruitment falsely projected from the surgeons' lack of equipoise to the patients' refusal to participate. This is clearly worth exploring in future research in H&N surgical trial recruitment. It may be perceived that our data are limited by recording the subjective opinion of the surgical teams. However, as it is often the pervading culture within surgery and attitude of surgeons to RCTs felt to be at issue, we feel that our data significantly inform this field.

An important reported barrier was the lack of time in the clinic to accommodate research. Although research resources are allocated by the Research Networks to best support the NIHR portfolio of studies, without doubt this has reflected historical practice and therefore presents a lag effect when portfolio studies are opened in new clinical fields. Parallel work is ongoing through GRIST, the National Cancer Research Network and the H&N Clinical Studies Group to identify centres where allocation of clinical sessions, research nurses and other resources will enhance portfolio recruitment in surgical trials. Clearly, NHS surgeons are busy, and will not only need to make trial recruitment as one of their priorities to succeed but also they must be adequately supported by research infrastructure.

The excessive complexity of patient information, perhaps combined with the educational level of many affected patients, was also flagged up as a significant problem. Although there is public and patient involvement at every level in these trials, patient information material may expand in complexity as a result of the input

from ethics committees and other regulatory structures. Further work may be needed to ensure that patient information is delivered in an appropriate manner to facilitate recruitment. In future work, it may be possible to further explore the contribution of socioeconomic/educational differences between H&N patients with cancer and other groups such as patients with breast cancer.

Other barriers to recruitment, perhaps less importantly, did vary between the three trials. For those trials where specific interventions were needed only for research, the availability and funding through excess treatment costs were important barriers. This highlights that the established NHS policy for such funding does not always resource appropriate research in practice. Additionally, the SEND trial presented more problems for equipoise and for patient-reported aversion to recruitment, perhaps confirming the interdependence of these two issues discussed above.

In summary, we have found that the most significant perceived barrier to trial recruitment in H&N cancer surgery is patient preference for one arm of the trial. This confirms the recent work in other surgical trials exploring treatment preferences[10 11] and emphasises the importance of exploring patients' views at the time of trial design. Further support and training for those taking consent may be helpful so that patients can explore their views and reach an informed decision about trial inclusion. There also appears to be insufficient resource in surgical clinics to enable effective trial recruitment and perhaps also a lack of incentives for surgeons to become involved in clinical research. These findings clarify the attitudes of surgeons towards RCTs and inform the basis of interventions to improve recruitment.

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