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Dissemination of trial results to participants in Phase III pragmatic clinical trials: an audit of trial investigators intentions.

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1 **Dissemination of trial results to participants in Phase III pragmatic clinical trials: an audit of trial**
2 **investigators intentions.**

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For peer review only

9 ABSTRACT

11 **Objective** To determine the proportion of Phase III clinical trials given a favourable opinion by a
12 research ethics committee in the UK that provided trial results to those who participated.

13 **Design** Audit of records.

14 **Setting** Phase III clinical trials registered on the Integrated Research Application System between the
15 1 January 2012 to 31 December 2017.

16 **Main outcome measures** Proportion of trials that intended to provide results to trial participants
17 compared against what trials reported at end of study.

18 **Results** Out of 1,404 phase III trials, 87.7% (n=1231) trials stated they intended to disseminate results
19 to participants while 12.3% (n=173) trials stated they would not. Out of these 1,231 trials, 18.8%
20 (n=231) trials intended to actively communicate trial results or a means of accessing results to their
21 participants with a further 80.5% (n=990) reporting passive intention to disseminate. Only 381 (31%)
22 trial teams that intended to feedback trial results reported they intended to involve patients or the
23 public during the design or conduct of the trial. Of the 370 End of Study Reports that could be accessed
24 ten explicitly mentioned activities related to dissemination of findings to participants with the majority
25 (74.9%) having no mention.

26 **Conclusions** Intention to disseminate results to trial participants amongst trial investigators is high,
27 however, reporting of appropriate feedback methods is lacking. In addition, mechanisms to ensure
28 intentions to disseminate trial results are translated into actual behaviour need to be put in place to
29 ensure those who participate in trials have the opportunity to find out about the results.

31 Article Summary

32 Strengths and limitations of this study

- 33 • First audit of the Integrated Research Application System (IRAS) to investigate trial
34 investigators intention to disseminate trial results to participants.
- 35 • Describes frequency of intention to disseminate and reported plans for dissemination.
- 36 • Links End of Study reports to original IRAS applications and provides a summary of overall
37 behaviours about reporting of dissemination of result sin said reports.
- 38 • Linkage with End of Study Reports to report actual behaviour regarding dissemination is
39 limited due to no explicit requirement from HRA to report this activity in final report.

41 **Key words:** *Research Transparency, Results Dissemination, Trial Conduct, Patient and Public*
42 *Involvement*

43 INTRODUCTION

44

45 Clinical trials and research are increasing in the UK. In 2018, a total of 870,250 participants took part
46 in NIHR CRN supported clinical research studies in England alone- marking an increase of over 140,000
47 over the previous year [1]. The cumulative cost of these studies was around £6 billion and is likely to
48 increase as the NHS Long Term Plan targets to include one million people taking part in research by
49 2023/24 [1]. With this growing trend in clinical research, there is a recognised need to promote
50 transparency and public involvement and engagement.

51

52 In 2008, a key review based on 28 empirical studies demonstrated that 90% of participants would
53 want to be informed of the results of the research that they were involved in [2]. Despite this interest
54 shown by participants, little is being done to provide them with results [3]. A survey on research
55 participant experience showed that 90% of respondents were happy with the information that they
56 received before or during the research. However, there was little indication that they were provided
57 with or made aware of the opportunity to access results after completion [4].

58

59 In order to encourage the dissemination of results, the Health Research Authority published guidelines,
60 recommending that all researchers communicate results to their study participants [5]. The guidelines
61 also recommend patient and public involvement (PPI) in all aspects of the research process [5]. This
62 refers to the involvement of patients and/or members of the public in the design or undertaking of
63 the research process [6]. An example of this would be patient input regarding the mode of
64 dissemination of results in order to improve the feedback process. These contributions can be very
65 valuable as they can provide an alternative perspective that the researchers may not have considered
66 and can ensure the materials are accessible to non-experts.

67

68 In the UK, applications for ethical approval are made through the Integrated Research Application
69 System (IRAS). The IRAS form includes questions regarding the researchers' intention to disseminate
70 results to participants as well as any intended PPI. Upon completion, the research team must then
71 submit a declaration of end of study to the research ethics committee (REC) followed by a final ethics
72 report within 12 months of the completion of the study. The final ethics report should confirm any
73 steps taken to disseminate results to participants. The guidelines also instruct researchers about the
74 information to be included in the patient's end of study information sheet, which should as a minimum
75 offer the results and specify when and how participants should expect to receive results.

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3 77 In addition, this national level guidance, there is international recognition of the ethical imperative
4
5 78 (specified within the Declaration of Helsinki) to offer results which is represented by the statement
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7 79 '*all medical research subjects should be given the option of being informed about the general outcome*
8
9 80 *and results of the study*' [7].
10

11 81
12 82 Whilst there is a need to provide results of any research study which a participant has contributed to,
13 83 providing results from clinical trials has salience in the current research transparency landscape [8].
14 84 Phase III clinical trials also hold a position of particular importance given all participants will have had
15 85 no choice in the treatment they received, many may not know what intervention they received,
16 86 several will have provided data through patient reported outcomes, and many are publicly funded. At
17 87 the very least, trial teams should be making the results of the studies to which these individuals
18 88 contribute to available and accessible to them in appropriate ways.
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25 90 This study aims to assess whether researchers in the UK intend to inform participants of the trial
26 91 results, plans for how results are provided, how patients are involved in this process, and finally,
27 92 whether those studies that intended to provide results report this activity in their end of study reports.
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33 95 **METHODS**

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36 97 **Inclusion Criteria**

37 98 This study included all applications on the Integrated Research Application System (IRAS) during the
38 99 period 1 January 2012 to 31 December 2017 where the research team had selected filter question 2
40 100 (defining the work as a clinical trial) and that had received a favourable Research Ethics Committee
41 101 (REC) opinion and carried out in the UK
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47 103 **Data Request and Extraction**

48 104 Information regarding the IRAS form submitted by researchers was requested from the Health
49 105 Research Authority (HRA). Data on study descriptors such as: IRAS Project ID; REC name; REC reference;
50 106 Study title; Protocol version and date; etc. In addition, data from project relevant questions, relating
51 107 to Patient and Public Involvement, plans for dissemination, and whether participants would receive
52 108 results, from within the IRAS form were requested, (see Box 1 for the specific questions and the data
53 109 types contained within them). On receipt of the data from IRAS, additional criteria were applied to
54 110 select Phase III clinical trials for inclusion (filtering to select only those studies that reported 'Yes' to
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3 111 the filter 'Therapeutic confirmatory trial (Phase III)'. The rationale for only including Phase III
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5 112 randomised controlled trials in this audit was due to Phase III trials largely collecting patient reported
6
7 113 outcomes, for which there may be more potential for demonstrable change and as such greater buy
8
9 114 in from participants to receive the overall results from the data collected.

10 115 The data items requested from IRAS were specified in the 'HARP Software Change/Management
11
12 116 Information Request Form'. In addition to the data contained within IRAS we also requested access to
13
14 117 final ethics reports (i.e. the End of Study reports) through the HRA Assessment Review Portal (HARP)
15
16 118 in order to confirm a match between information provided in the IRAS form about what was planned
17
18 119 for feeding back results to participants with what actually happened, as reported in the final report.
19
20 120 Final reports were identified by searching for specific REC reference identification numbers within
21
22 121 HARP.

122

123 **Box 1. Requested filter questions from IRAS form**

A14-1. In which aspects of the research process have you actively involved, or will involve, patients, service users, and/or their carers, or members of the public? Give details of involvement, or if none please justify the absence of involvement.

- Data provided: nominal data and open-ended text

A51. How do you intend to report and disseminate the results of the study?

- Data provided: nominal data and open-ended text

A53. Will you inform participants of the results? Please give details of how you will inform participants or justify if not doing so.

- Data provided: dichotomous data (yes/no) and open-ended text

124

125

126 **Data Analysis**

127 IRAS responses were summarised using descriptive statistics such as frequencies and percentages.
128 Measures of uncertainty were assessed using confidence intervals. Free text responses were
129 categorised using content analysis. Single level coding was applied, codes were developed iteratively
130 in discussion between team members and coding was performed by one team member. In order to
131 assess the involvement of trial teams in the act of dissemination, the intended means of dissemination
132 of results was categorised as being either active or passive:

133

- Active: The research team directly informed participants of the means by which the results could be accessed. For example, by a letter or by including a web link to the results.

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3 137 • Passive: Research team did not directly inform participants of a means to access trial results.
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5 138 For example, where the responsibility to forward the results was placed on the site team.
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8 140 **Patient and Public Involvement**

10 141 This audit forms part of a larger project that aims to develop recommendations for researchers on
11 142 how to report clinical trials results appropriately to participants (RECAP: researchregistry4085). There
12
13 143 are two patient partners on the Advisory group for the RECAP project who have contributed to this
14
15 144 sub-study. In addition, the HRA Patient and Public Involvement lead has also been involved in
16
17 145 conversations about this audit and had opportunity to comment and guide interpretation of the
18 146 results in advance of final analysis.
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21 148 **RESULTS**

22 149

23 150 **Data Mining**

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26 151 Data on a total of 6826 trials was received in the initial data set collated by the HRA based on the
27 152 requested filter questions. 1404 of these were identified as Phase III trials as pre-specified by the trial
28
29 153 team on the IRAS system (studies that reported 'Yes' to the filter 'Therapeutic confirmatory trial
30
31 154 (Phase III) – Figure 1).
32

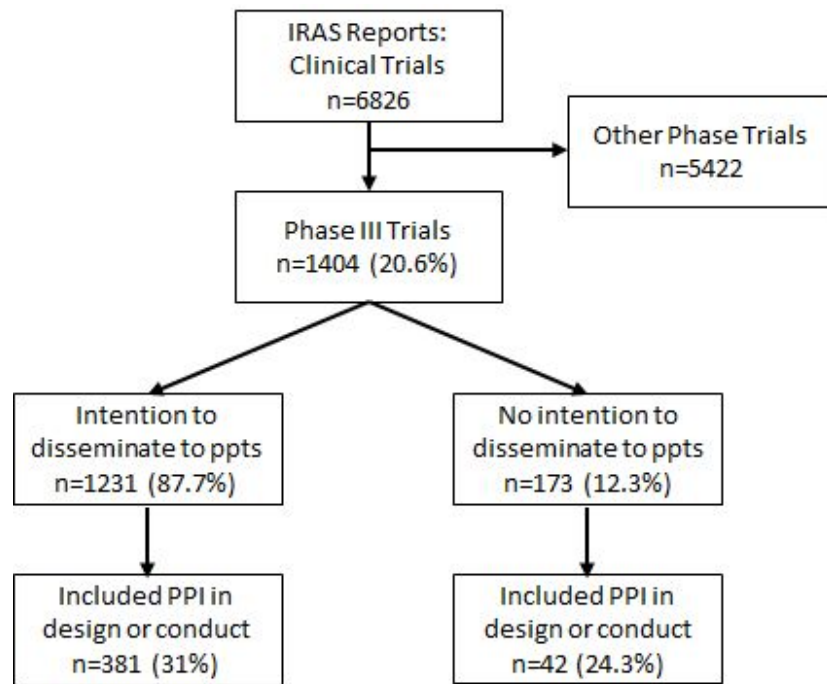
33 155

34 156 **Figure 1 Summary of search results**

35 157

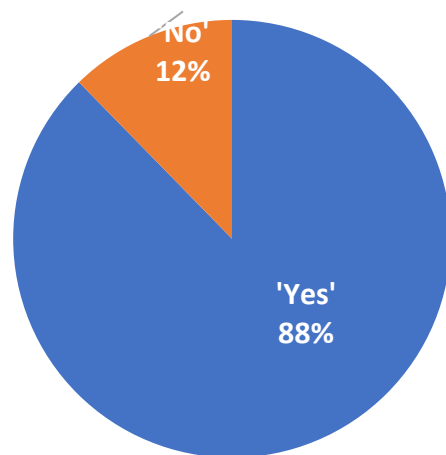
- 36
37 158 A. IRAS applications receiving a favourable opinion between 1 January 2012 to 31 December 2017
38 159 within the UK and self-identifying as a 'Clinical Trial'.
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B. Total number of Phase III Clinical Trials intending to disseminate (or not) results to trial participants.



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Intention to disseminate

167 A total of 1231 (87.7%) trials stated they intended to disseminate results to participants while 173
168 (12.3%) trials stated they would not. If answered yes, researchers were then asked to provide details
169 on how they intended to do so. Of those that said yes, we identified 231 (18.8%) as reporting an active
170 effort to disseminate results i.e. the trial team/sponsor actively made arrangements to provide
171 participants with results. The most commonly reported mode of active dissemination was directing
172 participants to a website with results. This was reported in 74 (32%) of trials that planned to actively
173 disseminate to participants. Some trials included this at the beginning of the trial in the Participant
174 Information Leaflet or at the end of participants involvement in the end of study information sheet.
175 Fifty-three (22.9%) trial teams stated that they intended to provide either lay summaries or

176 information sheets but did not specify any other information. Forty-four (19%) intended to send the
 177 results by mail directly to the participants. The 'other' category involves 4 (1.7%) trials that included
 178 reasons such as organising "dissemination events" and holding meetings with the participants. All
 179 responses are summarised in Table 1.

180

181 **Table 1. Summary of trial team responses regarding intention to disseminate**

Means of dissemination	Intention to disseminate results to participants	
	Yes	No
Active		
Web link	74 (32%)	-
Letter	44 (19%)	-
Information sheet	37 (16%)	-
Clinic appointment	23 (10%)	-
Lay patient summary	16 (6.9%)	-
Patient choice of mode of delivery	16 (6.9%)	-
PPI group	10 (4.3%)	-
Newsletter	5 (2.2%)	-
Email	2 (0.9%)	-
Other	4 (1.7%)	-
<i>Total</i>	<i>231 (18.8%)</i>	
Passive		
Trial linked staff	549 (55.4%)	72 (41.6%)
Participant initiated request	339 (34.2%)	49 (28.3%)
Public domain	84 (8.5%)	24 (13.9%)
Conference/publication	17 (1.7%)	-
Media	1 (0.1%)	-
Public representative meeting	1 (0.1%)	-
No reason stated	-	24 (13.9%)
Other	-	4 (2.3%)
<i>Total</i>	<i>991 (80.5%)</i>	<i>173 (100%)</i>
Unclear	9 (0.7%)	
TOTAL	1231	173

182

183

184 Within the trials that reported an intention to disseminate results to participants, we coded 991 as
 185 reporting a passive method to disseminate results i.e. there were no formal arrangements made to
 186 provide patients with access to the results. The most common method of passive dissemination stated
 187 the local site team, such as the study doctors or trial investigators, would provide results at their
 188 discretion. This accounted for 549 (55.4%) trials. Another 339 (34.2%) stated that results would be
 189 provided upon request but did not specify how the participants would be given the opportunity to
 190 request results. Finally, 84 (8.5%) intended to make the results available in the public domain but did
 191 not specify how the participants would be informed of or directed to these results.

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3 193 Responses coded as 'Unclear' (of which there were 9, 0.7%) either left the question unanswered or
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5 194 provided a vague statement. For example, 'Participants will be informed of the results post-study.'

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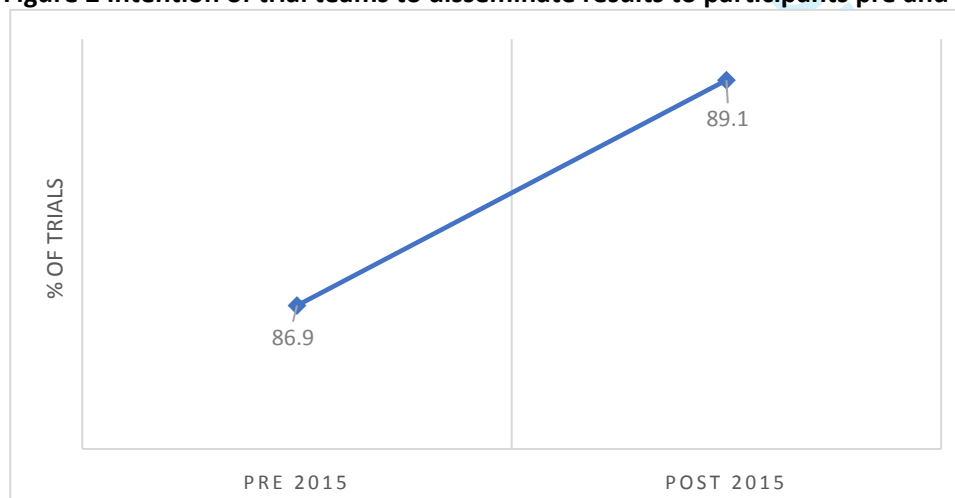
8 196 A total of 173 (12.3%) trials reported that they did not intend to provide participants with the results.
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10 197 Of these, 72 (41.6%) stated that there were no plans to disseminate results, but that study
11
12 198 investigators or study doctors may pass on the results. Forty-nine (28.3%) stated that results would
13
14 199 be provided if the participants expressed an interest or requested them. Twenty-four (13.9%)
15
16 200 provided no reason. Another 24 (13.9%) stated that results would be made available in the public
17
18 201 domain but not sent to participants directly. 'Other' (n=4, 2.3%) includes trials that mentioned the use
19
20 202 of patient groups to disseminate results or provided non-specific statements such as 'Patients will be
21
22 203 informed about the results of their study in an individual manner'.
23

24 204

25 205 In August 2015 the HRA introduced guidance for researchers on 'Information for participants at the
26
27 206 end of a study' [9]. Whilst not specifically about the content and how to provide feedback, the
28
29 207 guidance does provide a section on how results will be made available to participants. As such we
30
31 208 wanted to determine whether this guidance had any effect on trial team's intention to disseminate
32
33 209 results to participants. To investigate this we conducted a pre (before September 2015) and post
34
35 210 (after September 2015) guidance analysis to explore any effect on intention. There was a slight
36
37 211 increase in intention to report from pre-2015 to post-2015 (2.2%, 95% CI -1.3% to 5.7%). However,
38
39 212 this increase was small and whilst there is enough uncertainty to conclude that intention to report is
40
41 213 not getting worse, we cannot conclude with enough certainty that it is getting better (see Figure 2).
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43 214

44 215 **Figure 2 Intention of trial teams to disseminate results to participants pre and post HRA guidance**



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221 Patient and Public Involvement

222 We also wanted to determine whether those trials that planned to disseminate results to trial
 223 participants were better overall at including patients in the design and conduct of the trial. Therefore,
 224 we analysed whether and how the trials that intended to disseminate results included patients as
 225 partners in their studies.

226
 227 Within the sample of 1231 who planned to disseminate results to participants, 381 (31%) trial teams
 228 also reported they intended to involve patients or the public in the design or conduct of their trial.
 229 The largest proportion of PPI was observed in the dissemination phase with 227 trials accounting for
 230 59.6% while only 4.5% (n= 17) had input during the analysis phase. Elsewhere, 180 (47.2%) reported
 231 they would incorporate PPI in the design phase of the research; 123 (32.3%) had input during the
 232 undertaking of the trial; and 121 (31.7%) involved patients or public in the management phase (see
 233 Table 2). It is important to note that involvement was not mutually exclusive to one individual design
 234 or conduct category and researchers could select involvement across multiple categories.

235
 236 **Table 2. Researcher reported Patient Public Involvement in trial design and/or conduct**

Aspect of trial	IRAS reported PPI in design and/or conduct of trial			
	Intention to disseminate results to ppts (n=381)		No intention to participate results to participants (n=42)	
	Frequency	%	Frequency	%
Design	180	47.2	16	38.1
Management	121	31.7	6	14.3
Undertaking	123	32.3	28	66.7
Analysis	17	4.5	2	4.8
Dissemination	227	59.6	11	26.2

237 *Totals for % are greater than 100 as categories are not mutually exclusive and research teams could
 238 report PPI across several aspects of the research.

239
 240 Forty-two (24%) of the 173 trials that had no intention of disseminating results back to participants
 241 did report patient or public involvement in at least one aspect of the trial process. Within this sample
 242 of 42, undertaking the research was reported most frequently as involving PPI (n=28, 66.6%), followed
 243 by design (n=16, 38%), dissemination (n=11, 26%), management (n=6, 14.3%), and analysis (n=2, 4.7%).
 244 Again, it is important to note that involvement was not mutually exclusive to one category.

245
 246 A total of 850 (69%), from the 1231 trials that intended to disseminate result to participants, stated
 247 they would not be involving PPI partners at any stage of the research process. Among these, 244
 248 (28.7%) deemed PPI to be unnecessary due to the sufficient expertise present among the members of
 249 the research team or other sources e.g. 'It was felt that sufficient input had been gained from other
 250 sources.'. A further 213 (25.0%) trials responded that it was inappropriate to involve members of the

251 public due to the complex or experimental nature of the trial or the use of an unlicensed drug. One
 252 hundred and forty-five (16.6%) trials stated that all aspects of the research process were sole
 253 responsibility of the trial sponsor. One hundred and five (12.4%) trials did not provide an explanation
 254 for not doing so. 'Other' involved 34 (3.9%) trials that do not give a specific reason for the lack of PPI
 255 or simply describe the details of the trial itself. For example, 'No patients, services and/or their carers,
 256 or members of the public were involved with the design of the protocol'. Finally, 'Prescribed design'
 257 accounted for 12 (1.4%) of the responses, which refers to studies that are using previously
 258 implemented trial designs and who deemed PPI not necessary. Responses are summarised in Table 3.

259

260 **Table 3. Summary of responses to justification of no patient public involvement**

Reason	Frequency (n)	% of total
Sufficient Expertise	244	28.7
Sponsor Responsibility	145	17.1
Inappropriate – Experimental nature of trial	110	12.9
Unanswered	105	12.4
Inappropriate – complexity of trial	83	9.8
Commercial trial	82	9.6
Inappropriate – unprescribed drug	20	2.4
Confidentiality	15	1.8
Prescribed Research Design	12	1.4
Other	34	3.9
TOTALS	850	100

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262

263 **End of Study Report**

264 Data for the 1231 trials that intended to disseminate results was extracted from HARP to identify,
 265 firstly, whether these studies submitted an End of Study report. Several trials (517 (42%)) were still in
 266 progress when the data was requested while 90 trials (7.3%) had been terminated or abandoned and
 267 as such no End of Study reports were available for these trials. Of the 624 completed trials, 370 (59.3%
 268 of completed trials and 30% total sample) submitted a final ethics report while 127 (20.4% of
 269 completed trials and 10.3% of total sample) failed to do so and 127 (20.4% of completed trials and
 270 10.3% of total sample) were still within the 12-month post study period and were due to submit their
 271 final ethics reports. (Table 4).

272

273 **Table 4. End of Study Report Status**

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Report Status	Frequency (n)	% of total	
Completed trials	Submitted	370	30.0
	Not submitted	127	10.3
	Incomplete HARP data ²	127	10.3
Trial in progress ¹	517	42.0	
Trial terminated/abandoned	90	7.3	
TOTAL	1231	100	

¹Trial in progress: trial currently

recruiting or in follow up, or, not yet started, or, trial complete and not reported but has up to 12 months to report.

²Incomplete HARP data: HARP has trial registered but is incomplete. e.g. does not clearly state that trial ever started/little or no documentation uploaded to HARP.

Of the 370 studies that did submit an End of Study report, the majority of these (277, 74.9%) did not mention any arrangements made regarding the dissemination of trial results back to participants yet all expressed intention to do so on the original IRAS application. Six studies (1.6%) provided a copy of the lay summary or referred to it in the report or the cover letter. Evidence of other strategies used to inform participants of the trial results were also poorly represented with 2 (0.5%) studies providing the patient end of study sheet, 1(0.3%) offering a final follow up visit, and another 1 (0.3%) mentioning presentation at a scientific conference. The reports of 83 (22.4%) trials were inaccessible due to some requiring passwords or email access or yet to be uploaded by the REC to the HARP system. See Table 5.

Table 5. Reporting of dissemination of result to trial participants in End of Study reports

Dissemination of results reported	2013	2014	2015	2016	2017	2018	2019	TOTAL (n/%)
No mention	1	23	42	58	65	53	35	277 (74.9)
Confirmation of Lay summary/letter ¹	-	-	-	-	1	3	2	6 (1.6)
Patient end of study sheet attached	-	-	-	-	-	1	1	2 (0.5)
Follow up visit	-	-	-	-	-	-	1	1 (0.3)
Presentation at scientific conference	-	-	1	-	-	-	-	1 (0.3)
Report inaccessible ²	5	3	7	3	16	32	17	83 (22.4)
TOTAL	6	26	50	61	82	89	56	370 (100)

¹ Confirmation of lay summary/letter either as an attached copy or mentioned in final report/cover letter.

² Report inaccessible: Reports that require password/email access or have to be uploaded by the REC.

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7 3088 309 **DISCUSSION**9
10 31011 311 **Key findings**

12 312 This study reports the first audit of researcher intentions and self-reported behaviours with regard to
13 313 dissemination of clinical trial results to participants across the UK using reports within the HRA
14 314 regulatory system. We have found that while the majority (1231, 87.7%) of applications stated that
15 315 they intended to disseminate trial results to the participant, less than 20% (231, 18.8%) specified some
16 316 form of direct 'active' communication with their participants. The majority of trial teams (80.5%) left
17 317 the responsibility of participants accessing trial results with the clinical care team or on the participant
18 318 themselves. The other key finding relates to the dissemination behaviour reported by trial teams in
19 319 their End of Study report, which demonstrated that 59.4% of completed trials had submitted an End
20 320 of Study report compared to 20.4% that had not. However, the majority (74.9%) of End of Study
21 321 Reports did not mention any arrangements for the provision of trial results to participants.

22 322

23 323 The findings from our study show the potential variability in reporting trial results back to participants
24 324 with several trial teams not doing so, which is in line with findings from previous studies [10]. Also,
25 325 the variability we identified with regard to how the results would be provided (i.e. paper based, web-
26 326 link, face-to-face meeting) have also been documented in the literature [2]. However, variability of
27 327 this type is much less problematic (and often warranted) than that for whether the results will be
28 328 offered at all. The planned changes from the HRA stating they will change the IRAS question from
29 329 'whether' results will be disseminated to 'when and how' is welcome but research teams will still
30 330 require guidance in the what, how and when of dissemination [5].

31 331

32 332 Another interesting finding is the similarity between the responses provided in the applications that
33 333 intended to provide results to participants and those that did not. Collectively, 72% of the applications
34 334 that stated they intended to provide results relied on either site staff to provide results or the
35 335 participants to request the results themselves. Interestingly, these two categories of responses also
36 336 account for nearly 70% of those applications that responded with 'No' to intention to disseminate
37 337 results. In certain cases, an identical response was provided as justification for intention and no
38 338 intention. For instance, 'Investigators will be informed of the study results and may pass on the details
39 339 to participant' was a response that was observed in both the 'yes' and 'no' responses and in some

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3 340 instances was done in applications submitted by the same sponsor. This raises a concern that the
4
5 341 question may be interpreted differently by different researchers and that at a conceptual level there
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7 342 is a misunderstanding about what constitutes appropriate methods of disseminating results.
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9 343 Explanatory guidance notes within the IRAS system to ensure how researchers are expected to
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11 344 operationalise and implement the dissemination of results to trial participants may help to resolve
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13 345 some of this lack of continuity.

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15 347 It is disappointing to see that 69% of the trials included in our audit had no intention to include the
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17 348 public at any stage of the research. Nearly 10% of the 850 trials deemed it inappropriate to include
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19 349 the public due to the complexity of the trial. These findings also echo results from an earlier audit of
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21 350 patient involvement in IRAS applications [11]. Particular aspects or types of research may indeed be
22
23 351 difficult for a lay person to understand; however, members of the public may still be able to contribute
24
25 352 to the participant enrolment or result dissemination phase [12]. A review of publicly funded trials to
26
27 353 explore how PPI was included in grant applications identified that most studies intended to have some
28
29 354 form of PPI input [12]. This contrasts with the findings of this audit and others and may reflect the
30
31 355 requirement of involvement of patients and/or the public as a condition of funding approval. This
32
33 356 raises the question as to whether there could be more linkage between funders to ensure that there
34
35 357 is consistency in intentions with regards to involvement and potentially dissemination.

33 358

35 359 Our study highlights that most End of Study reports do not mention dissemination of results to their
36
37 360 participants. However, this may not be surprising given the current guidance is not directive and
38
39 361 states', and arrangements for publication or dissemination of the research, including any feedback to
40
41 362 participants' [13]. Therefore, more explicit guidance from the Health Research Authority to include
42
43 363 information on dissemination of result to trial participants in the End of Study Report should be
44
45 364 implemented. The changes planned by the HRA as part of their Transparency Agenda will require
46
47 365 sponsors to submit a lay summary of the trial results and will attend to aspects of this [5]. This could
48
49 366 be strengthened by guidance on the what the content of the Lay Summary should cover.

48 367

50 368 A recent study that surveyed teams that had published trials (involving human participants and
51
52 369 enrolling individual patients) during 2014-2015 found only 27% of their eligible sample had
53
54 370 disseminated results back to participants with a further 13% planning to do so. This study reported a
55
56 371 range of barriers the trial teams identified with regard to disseminating results and summarised these
57
58 372 as: researchers perceptions of what interests patients and what they understand; challenges reaching
59
60 373 patients; which patients to share with; need for early planning and resource; researcher motivations

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2
3 374 and situational expectations; type of results to share; and, researcher specific reasons for not
4
5 375 disseminating [10]. The authors propose some helpful suggestions targeting multiple players (such as
6
7 376 increased scrutiny from ethics review boards, support from journals, and development of standards
8
9 377 and training) with the aim of improving practice.

10 378
11 379 More directive guidance, like the planned changes mentioned above, is required from the Health
12
13 380 Research Authority is required if we plan to change researcher's behaviour with regard to
14
15 381 disseminating results of trial to those who participated. The existing guidance published in 2015 did
16
17 382 not seem to impact on intentions to disseminate results. Therefore, the current approach of requiring
18
19 383 research teams to submit a Lay Summary at the end of the study seems more appropriate. It would
20
21 384 be helpful to go one step further and request sponsor to inform the HRA when and how those results
22
23 385 have been offered or disseminated to participants.

23 386

25 387 **Strengths and limitations**

26 388 This is the first audit of ethics applications reporting intention to disseminate results of trials to those
27
28 389 who participated. Set within a 5-year time frame we included a large sample (=1404) of phase III trials,
29
30 390 including a range of clinical populations, interventions, comparators, outcomes, and supported by a
31
32 391 range of funders. Other IRAS audits have been competed to assess registration of clinical trials given
33
34 392 a favourable opinion by UK research ethics committees, which also demonstrated the value of audits
35
36 393 of this type to assess current regulatory practice [14]. However, there were limitations to our
37
38 394 approach, principally that the IRAS data reports intention and not actual behaviour. There is evidence
39
40 395 from health psychology that intention only explain 36% of the variance in behaviour and as such
41
42 396 changing intentions does not necessarily engender behaviour change [15]. In other words, the 88% of
43
44 397 studies reporting they intend to disseminate results will likely be a much lower proportion that
45
46 398 actually do it. The other limitation to our study was that we relied on the identification of phase of
47
48 399 trial from trial teams.

47 400

48 401 **Conclusion**

49 402 Despite the 2015 HRA guidelines on end of study information, compliance rates are low with regards
50
51 403 to intention for dissemination of trial results to those who participated versus actual behaviour. It is
52
53 404 likely that this might change with the recent publication of the HRAs transparency agenda. One of the
54
55 405 key focuses of this strategy is 'letting research participants know about the results of the research'.
56
57 406 Literature regarding the most effective means of communicating results, particularly in the UK is
58
59 407 limited as is the impact of involving patient partners in the dissemination process. Hence, there is
60

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2
3 408 potential to conduct more embedded methodological research in these areas in order to identify best
4
5 409 practice about the what, how and when of disseminating trial result to participants.
6
7 410

8 411 **Acknowledgments**

9
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11
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13
14 414 progress and initial results of the study (specifically, Juliet Tizzard and Jim Elliott). Thanks also to
15
16 415 Graeme Maclennan for analysis advice.
17
18 416

18 417 **Contributors**

19
20 418 HB wrote the first draft of the study protocol. KG and MZR contributed to design of the project and
21
22 419 development of the protocol. MZR and KG conducted data analysis. All authors (MZR, HB, KG)
23
24 420 commented on the results. MZR wrote the first draft of the manuscript. All authors approved the final
25
26 421 version of the manuscript.
27
28 422

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31
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33
34 426 Masters in Public Health degree.
35
36 427

36 428 **Competing interests**

37
38 429 This audit forms part of a larger project that aims to develop recommendations for how to
39
40 430 appropriately feedback trial results to those who participated in them. This overarching project is
41
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43
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45
46 433 (MR/L01193X/1).
47
48 434

48 435 **Patient consent for publication**

49
50 436 Not required
51
52 437

52 438 **Ethics approval**

53
54 439 Not required
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56 440

56 441 **Data Sharing Statement**

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442 Data requests should be made to the Health Research Authority.

443

444 **Provenance and peer review**

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BMJ Open

Dissemination of trial results to participants in Phase III pragmatic clinical trials: an audit of trial investigators intentions.

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Primary Subject Heading:	Ethics
Secondary Subject Heading:	Health services research
Keywords:	Clinical trials < THERAPEUTICS, MEDICAL ETHICS, Clinical audit < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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3 1 **Dissemination of trial results to participants in Phase III pragmatic clinical trials: an audit of trial**
4 **investigators intentions.**
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9 ABSTRACT

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11 **Objective** To determine the proportion of Phase III clinical trials given a favourable opinion by a
12 research ethics committee in the UK that provided trial results to those who participated.

13 **Design** Audit of records.

14 **Setting** Phase III clinical trials registered on the UK's research permissions system (Integrated Research
15 Application System) between the 1 January 2012 to 31 December 2017.

16 **Main outcome measures** Proportion of trial investigators that intended to provide results to trial
17 participants compared against what trials reported to ethics committees at end of study.

18 **Results** Out of 1,404 Phase III trials, 87.7% (n=1231) trials stated they intended to disseminate results
19 to participants while 12.3% (n=173) trials stated they would not. Out of these 1,231 trials, 18.8%
20 (n=231) trials intended to actively communicate trial results or a means of accessing results to their
21 participants, a further 80.5% (n=991) reported passive intention to disseminate, and for the
22 remainder (n=9) the process was unclear. Of the 370 End of Study Reports (30% of all included studies)
23 that could be accessed ten (2.7%) explicitly mentioned activities related to dissemination of findings
24 to participants with the majority (74.9%) having no mention and a further 22.4% of reports not being
25 accessible. Of the 10 which did report dissemination of results to participants the majority (n=6) were
26 through a lay summary or letter.

27 **Conclusions** Reported intention to disseminate results to trial participants amongst trial investigators
28 is high, however, reporting of feedback methods is lacking. In addition, mechanisms to ensure
29 intentions to disseminate trial results are translated into actual behaviour need to be put in place to
30 ensure those who participate in trials have the opportunity to find out about the results.

31

32 Article Summary

33 Strengths and limitations of this study

- 34 • First audit of the Integrated Research Application System (IRAS) to investigate trial
35 investigators reported intention to disseminate trial results to participants.
- 36 • Describes frequency of intention to disseminate and reported plans for dissemination.
- 37 • Links End of Study reports to original IRAS applications and provides a summary of overall
38 behaviours about reporting of dissemination of results in said reports.
- 39 • Linkage with End of Study Reports to report actual behaviour regarding dissemination is
40 limited due to no explicit requirement from HRA to report this activity in final report.

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3 42 Key words: *Research Transparency, Results Dissemination, Trial Conduct, Patient and Public*
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5 43 *Involvement*
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44 INTRODUCTION

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46 Clinical trials and research are increasing in the UK. In 2018, a total of 870,250 participants took part
47 in National Institute for Health Research Clinical Research Network (NIHR CRN) supported clinical
48 research studies in England alone- marking an increase of over 140,000 over the previous year [1]. The
49 cumulative cost of these studies was around £6 billion and is likely to increase as the NHS Long Term
50 Plan targets to include one million people taking part in research by 2023/24 [1]. This increase in
51 participants numbers has the potential to translate into significant improvement in delivery of
52 healthcare as long as findings are disseminated to those with responsibility to make a change (policy
53 makers) and the end users of the services (patients and health care professionals).

54 In 2008, a key review based on 28 empirical studies demonstrated that 90% of participants would
55 want to be informed of the results of the research that they were involved in [2]. Despite this interest
56 shown by participants, little is being done to provide them with results [3]. A survey on research
57 participant experience showed that 90% of respondents were happy with the information that they
58 received before or during the research. However, there was little indication that they were provided
59 with or made aware of the opportunity to access results after completion [4]. This lack of attention to
60 meeting expectations of research participants is not acceptable. When aligned with recent initiatives
61 to improve research integrity through ensuring trials are registered and that their results are published,
62 it seems an obvious next step to make sure those who participated in them (and who which without
63 they would not be possible) are informed of the results.

64

65 In order to encourage the dissemination of results, the Health Research Authority (HRA, whose core
66 purpose it 'to protect and promote the interests of patients and public in health and social care
67 research' in the UK) published guidelines, recommending that all researchers communicate results to
68 their study participants and at the very least offer the results[5].The guidelines also recommend
69 patient and public involvement (PPI) in all aspects of the research process [5]. This refers to the
70 involvement of patients and/or members of the public in the design or undertaking of the research
71 process [6]. An example of this would be patient input regarding the mode of dissemination of results
72 in order to improve the feedback process. These contributions can be very valuable as they can
73 provide an alternative perspective that the researchers may not have considered and can ensure the
74 materials are accessible to non-experts. Unlike the dissemination of results, which is not mandatory
75 for Phase III trials, the inclusion of PPI in the research process is mandated by funding bodies as a
76 prerequisite to obtaining funding.

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3 78 In the UK, applications for ethical approval are made through the Integrated Research Application
4 79 System (IRAS). The IRAS form includes questions regarding the researchers' intention to disseminate
5 80 results to participants as well as any intended PPI. Upon completion, the research team must then
6 81 submit a declaration of end of study to the research ethics committee (REC) followed by a final ethics
7 82 report within 12 months of the completion of the study (the End of Study Report). The final ethics
8 83 report should confirm any steps taken to disseminate results to participants [7]. The guidelines also
9 84 instruct researchers about the information to be included in the patient's end of study information
10 85 sheet, which should as a minimum offer the results and specify when and how participants should
11 86 expect to receive results.
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20 88 In addition, this national level guidance, there is international recognition of the ethical imperative
21 89 (specified within the Declaration of Helsinki) to offer results which is represented by the statement
22 90 '*all medical research subjects should be given the option of being informed about the general outcome*
23 91 *and results of the study*' [8].
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28 93 Whilst there is a need to provide results of any research study which a participant has contributed to,
29 94 providing results from clinical trials has salience in the current research transparency landscape [9].
30 95 Phase III clinical trials also hold a position of particular importance given all participants will have had
31 96 no choice in the treatment they received, many may not know what intervention they received,
32 97 several will have provided data through patient reported outcomes, and many are publicly funded. At
33 98 the very least, trial teams should be making the results of the studies to which these individuals
34 99 contribute to available and accessible to them in appropriate ways.
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41 101 This study aims to assess whether researchers in the UK intend to inform participants of the trial
42 102 results, plans for how results are provided, how patients are involved in this process, and finally,
43 103 whether those trial teams that intended to provide results report this activity in their end of study
44 104 reports.
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51 107 **METHODS**

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53 109 **Inclusion Criteria**

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57 110 This study included all applications on the Integrated Research Application System (IRAS) during the
58 111 period 1 January 2012 to 31 December 2017 where the research team had selected filter question 2
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3 112 (defining the work as a clinical trial) and that had received a favourable Research Ethics Committee
4 113 (REC) opinion and carried out in the UK. IRAS is the UK's online system for the permissions and
5 114 approvals for health, social and community care research.
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10 116 **Data Request and Extraction**

11 117 Information regarding the IRAS form submitted by researchers was requested from the Health
12 118 Research Authority (HRA). Specific data on study descriptors such as: IRAS Project ID; REC name; REC
13 119 reference; Study title; Protocol version and date; etc was requested. In addition, data from project
14 120 relevant questions, relating to Patient and Public Involvement, plans for dissemination, and whether
15 121 participants would receive results, from within the IRAS form were requested, (see Box 1 for the
16 122 specific questions and the data types contained within them). On receipt of the data from IRAS,
17 123 additional criteria were applied to select Phase III clinical trials for inclusion (filtering to select only
18 124 those studies that reported 'Yes' to the filter 'Therapeutic confirmatory trial (Phase III)'. The rationale
19 125 for only including Phase III randomised controlled trials in this audit was due to Phase III trials largely
20 126 collecting patient reported outcomes, for which there may be more potential for demonstrable
21 127 change in practice and as such greater buy in from participants to receive the overall results from the
22 128 data collected.
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33 130 **Box 1. Requested filter questions from IRAS form**

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36 **A14-1. In which aspects of the research process have you actively involved, or will involve, patients, service users, and/or their carers, or members of the public? Give details of involvement, or if none please justify the absence of involvement.**

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40 - Data provided: nominal data and open-ended text

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42 **A51. How do you intend to report and disseminate the results of the study?**

- 43 - Data provided: nominal data and open-ended text

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45 **A53. Will you inform participants of the results? Please give details of how you will inform participants or justify if not doing so.**

- 46
47 - Data provided: dichotomous data (yes/no) and open-ended text
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51 132 The data items requested from IRAS were specified in the 'HARP Software Change/Management
52 133 Information Request Form'. In addition to the data contained within IRAS we also requested access to
53 134 final ethics reports (i.e. the End of Study reports) through the HRA Assessment Review Portal (HARP)
54 135 in order to confirm a match between information provided in the IRAS form about what was planned
55 136 for feeding back results to participants with what actually happened, as reported in the final report.
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3 137 Final reports were identified by searching for specific REC reference identification numbers within
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5 138 HARP.

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8 140 **Data Analysis**

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10 141 IRAS responses which provided nominal data were summarised using descriptive statistics such as
11 142 frequencies and percentages e.g. 'Will you inform participants of the results? – Yes/No?'. Free text
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13 143 responses were categorised using content analysis. Single level coding was applied, codes were
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15 144 developed iteratively in discussion between team members and coding was performed by one team
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17 145 member. In order to assess the involvement of trial teams in the act of dissemination, our team
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19 146 categorised the intended means of dissemination of results as being either active or passive:

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22 148 • Active: The trial team directly informed participants of the means by which the results could
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24 149 be accessed. For example, by a letter or by including a web link to the results.

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26
27 151 • Passive: Trial team did not directly inform participants of a means to access trial results. For
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29 152 example, where the responsibility to forward the results was placed on the site team.

30 153

31 154 **Patient and Public Involvement**

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33 155 This audit forms part of a larger project that aims to develop recommendations for researchers on
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35 156 how to report clinical trial results appropriately to participants (RECAP: researchregistry4085). There
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37 157 are two patient partners on the Advisory group for the RECAP project who have contributed to this
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39 158 sub-study through discussion of results at team meetings. In addition, the HRA Patient and Public
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41 159 Involvement lead has also been involved in conversations about this audit and had opportunity to
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43 160 comment and guide interpretation of the results in advance of final analysis.

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45 162 **RESULTS**

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48 164 **Data Mining**

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50 165 Data on a total of 6826 trials (which had received a favourable opinion from a REC) was received in
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52 166 the initial data set collated by the HRA based on the requested filter questions. 1404 of these were
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54 167 identified as Phase III trials as pre-specified by the trial team on the IRAS system (studies that reported
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56 168 'Yes' to the filter 'Therapeutic confirmatory trial (Phase III) – Figure 1).

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58 170 **Intention to disseminate**

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3 171 A total of 1231 (87.7%) trial teams stated they intended to disseminate results to participants while
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5 172 173 (12.3%) trials stated they would not. Researchers were then asked to provide details on how they
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7 173 intended to do so. Of those that said yes, we identified 231 (18.8%) as reporting an active effort to
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9 174 disseminate results i.e. the trial team/sponsor actively made arrangements to provide participants
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11 175 with results. The most commonly reported mode of active dissemination was directing participants to
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13 176 a website with results (see Table 1). This was reported in 74 (32%) of trials that planned to actively
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15 177 disseminate to participants. Some trials included this at the beginning of the trial in the Participant
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17 178 Information Leaflet or at the end of participants involvement in the end of study information sheet.
18
19 179 Fifty-three (22.9%) trial teams stated that they intended to provide either lay summaries or
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21 180 information sheets but did not specify any other information. Forty-four (19%) intended to send the
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23 181 results by mail directly to the participants. The 'other' category involves 4 (1.7%) trials that included
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25 182 reasons such as organising "dissemination events" and holding meetings with the participants..
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Table 1. Summary of trial team responses regarding intention to disseminate

Means of dissemination	Intention to disseminate results to participants	
	Yes	No
Active		
Provision of web link to results	74 (32%)	-
Postal letter	44 (19%)	-
Patient information sheet	37 (16%)	-
Clinic appointment	23 (10%)	-
Lay patient summary	16 (6.9%)	-
Patient choice of mode of delivery	16 (6.9%)	-
PPI group	10 (4.3%)	-
Newsletter	5 (2.2%)	-
Email	2 (0.9%)	-
Other (e.g. face-to-face meetings)	4 (1.7%)	-
<i>Total</i>	<i>231 (18.8%)</i>	
Passive		
Trial linked staff (e.g. discretion of study doctor)	549 (55.4%)	72 (41.6%)
Participant initiated request	339 (34.2%)	49 (28.3%)
Public domain (trial website)	84 (8.5%)	24 (13.9%)
Conference/scientific publication	17 (1.7%)	-
Media	1 (0.1%)	-
Public representative meeting	1 (0.1%)	-
No reason stated	-	24 (13.9%)
Other	-	4 (2.3%)
<i>Total</i>	<i>991 (80.5%)</i>	<i>173 (100%)</i>
Unclear	9 (0.7%)	
TOTAL	1231	173

185

1
2
3 186 Within the trials whose teams reported an intention to disseminate results to participants, we coded
4
5 187 991 as reporting a passive method to disseminate results i.e. there were no formal arrangements
6
7 188 made to provide patients with access to the results. The most common method of passive
8
9 189 dissemination stated the local site team, such as the study doctors or trial investigators, would provide
10
11 190 results at their discretion. This accounted for 549 (55.4%) trials. Another 339 (34.2%) trial teams stated
12
13 191 that results would be provided upon request but did not specify how the participants would be given
14
15 192 the opportunity to request results. Finally, 84 (8.5%) intended to make the results available in the
16
17 193 public domain but did not specify how the participants would be informed of or directed to these
18
19 194 results.

18 195
19
20 196 Responses coded as 'Unclear' (of which there were 9, 0.7%) either left the question unanswered or
21
22 197 provided a vague statement. For example, 'Participants will be informed of the results post-study.'

23 198
24
25 199 A total of 173 (12.3%) trial teams reported that they did not intend to provide participants with the
26
27 200 results. Of these, 72 (41.6%) stated that there were no plans to disseminate results, but that study
28
29 201 investigators or study doctors may pass on the results. Forty-nine (28.3%) stated that results would
30
31 202 be provided if the participants expressed an interest or requested them. Twenty-four (13.9%)
32
33 203 provided no reason. Another 24 (13.9%) stated that results would be made available in the public
34
35 204 domain but not sent to participants directly. 'Other' (n=4, 2.3%) includes trials that mentioned the use
36
37 205 of patient groups to disseminate results or provided non-specific statements such as 'Patients will be
38
39 206 informed about the results of their study in an individual manner'.

40 207 41 208 42 209 **Patient and Public Involvement**

43 210 We also wanted to determine whether those trials that planned to disseminate results to trial
44
45 211 participants were better overall at including patients in the design and conduct of the trial. Therefore,
46
47 212 we analysed whether and how the trial teams that intended to disseminate results included patients
48
49 213 as partners in their studies.

50 214
51 215 Within the sample of 1231 who planned to disseminate results to participants, 381 (31%) trial teams
52
53 216 also reported they intended to involve patients or the public in the design or conduct of their trial.
54
55 217 The largest proportion of PPI was observed in the dissemination phase with 227 trials accounting for
56
57 218 59.6% while only 4.5% (n= 17) of trial teams proposed input during the analysis phase. Elsewhere, 180
58
59 219 (47.2%) reported they would incorporate PPI in the design phase of the research; 123 (32.3%) would
60
220 seek input whilst the undertaking of the trial; and 121 (31.7%) proposed to involve patients or public

221 in the management phase (see Table 2). It is important to note that involvement was not mutually
 222 exclusive to one individual design or conduct category and researchers could select involvement
 223 across multiple categories.

224

225 **Table 2. Researcher reported Patient Public Involvement in trial design and/or conduct**

Aspect of trial	IRAS reported PPI in design and/or conduct of trial			
	Intention to disseminate results to ppts (n=381)		No intention to participate results to participants (n=42)	
	Frequency	%	Frequency	%
Design	180	47.2	16	38.1
Management	121	31.7	6	14.3
Undertaking	123	32.3	28	66.7
Analysis	17	4.5	2	4.8
Dissemination	227	59.6	11	26.2

226 *Totals for % are greater than 100 as categories are not mutually exclusive and research teams could report PPI
 227 across several aspects of the research.

228

229 Forty-two (24%) of the 173 trial teams that had no intention of disseminating results back to
 230 participants did report patient or public involvement in at least one aspect of the trial process. Within
 231 this sample of 42, undertaking the research was reported most frequently as involving PPI (n=28,
 232 66.6%), followed by design (n=16, 38%), dissemination (n=11, 26%), management (n=6, 14.3%), and
 233 analysis (n=2, 4.7%). Again, it is important to note that involvement was not mutually exclusive to one
 234 category.

235

236 A total of 850 (69%), from the 1231 trial teams that intended to disseminate result to participants,
 237 stated they would not be involving PPI partners at any stage of the research process. Among these,
 238 244 (28.7%) deemed PPI to be unnecessary due to the sufficient expertise present among the
 239 members of the research team or other sources e.g. 'It was felt that sufficient input had been gained
 240 from other sources.'. A further 213 (25.0%) trials responded that it was inappropriate to involve
 241 members of the public due to the complex or experimental nature of the trial or the use of an
 242 unlicensed drug. One hundred and forty-five (16.6%) trials stated that all aspects of the research
 243 process were sole responsibility of the trial sponsor. One hundred and five (12.4%) trials did not
 244 provide an explanation for not doing so. 'Other' involved 34 (3.9%) trials that do not give a specific
 245 reason for the lack of PPI or simply describe the details of the trial itself. For example. 'No patients,
 246 services and/or their carers, or members of the public were involved with the design of the protocol'.
 247 Finally, 'Prescribed design' accounted for 12 (1.4%) of the responses, which refers to studies that are
 248 using previously implemented trial designs and who deemed PPI not necessary. Responses are
 249 summarised in Table 3.

250

251 **Table 3. Summary of responses to justification of no patient public involvement**

Reason	Frequency (n)	% of total
Sufficient Expertise	244	28.7
Sponsor Responsibility	145	17.1
Inappropriate – Experimental nature of trial	110	12.9
Unanswered	105	12.4
Inappropriate – complexity of trial	83	9.8
Commercial trial	82	9.6
Inappropriate – unprescribed drug	20	2.4
Confidentiality	15	1.8
Prescribed Research Design	12	1.4
Other	34	3.9
TOTALS	850	100

252

253

254 **End of Study Report**

255 Data for the 1231 trial teams that intended to disseminate results was extracted from HARP to identify,
 256 firstly, whether these studies submitted an End of Study report. A large proportion of trials (517 (42%))
 257 were still in progress when the data was requested while 90 trials (7.3%) had been terminated or
 258 abandoned and as such no End of Study reports were available for these trials. Of the 624 completed
 259 trials, 370 (59.3% of completed trials and 30% total sample) submitted a final ethics report, while 127
 260 (20.4% of completed trials and 10.3% of total sample) failed to do so and 127 (20.4% of completed
 261 trials and 10.3% of total sample) had incomplete data registered within the HARP system making
 262 analysis difficult. (Table 4).

263 **Table 4. End of Study Report Status**

Report Status	Frequency (n)	% of total	
Completed trials	Submitted	370	30.0
	Not submitted	127	10.3
	Incomplete HARP data ²	127	10.3
Trial in progress ¹	517	42.0	
Trial terminated/abandoned	90	7.3	
TOTAL	1231	100	

274 ¹Trial in progress: trial currently recruiting or in follow up, or, not yet started, or, trial complete and not
 275 reported but has up to 12 months to report.

276 ²Incomplete HARP data: HARP has trial registered but is incomplete. e.g. does not clearly state that trial ever
 277 started/little or no documentation uploaded to HARP.

278

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280

281 Of the 370 studies that did submit an End of Study report, the majority of the trial teams (277, 74.9%)

282 did not mention any arrangements made regarding the dissemination of trial results back to

283 participants yet all expressed intention to do so on the original IRAS application. Six studies (1.6%)
 284 provided a copy of the lay summary or referred to it in the report or the cover letter. Evidence of other
 285 strategies used to inform participants of the trial results were also poorly represented with 2 (0.5%)
 286 studies providing the patient end of study sheet, 1(0.3%) offering a final follow up visit, and another
 287 1 (0.3%) mentioning presentation at a scientific conference. Whilst indicating the End of Study Reports
 288 had been uploaded, the reports of 83 (22.4%) trials were inaccessible due to some requiring
 289 passwords or email access or yet to be uploaded by the REC to the HARP system. Therefore, details
 290 from these reports could not be extracted or included in the analysis See Table 5.

291

292 **Table 5. Reporting of dissemination of result to trial participants in End of Study reports**

293

Dissemination of results reported	2013	2014	2015	2016	2017	2018	2019	TOTAL (n/%)
No mention	1	23	42	58	65	53	35	277 (74.9)
Confirmation of Lay summary/letter ¹	-	-	-	-	1	3	2	6 (1.6)
Patient end of study sheet attached	-	-	-	-	-	1	1	2 (0.5)
Follow up visit	-	-	-	-	-	-	1	1 (0.3)
Presentation at scientific conference	-	-	1	-	-	-	-	1 (0.3)
Report inaccessible ²	5	3	7	3	16	32	17	83 (22.4)
TOTAL	6	26	50	61	82	89	56	370 (100)

294 ¹ Confirmation of lay summary/letter either as an attached copy or mentioned in final report/cover letter.295 ² Report inaccessible: Reports that require password/email access or have to be uploaded by the REC.

296

297

298 **DISCUSSION**

299

300 **Key findings**

301 This study reports the first audit of researcher intentions and self-reported behaviours with regard to
 302 dissemination of clinical trial results to participants across the UK using reports within the HRA
 303 regulatory system. We have found that while the majority (1231, 87.7%) of trial teams stated in their
 304 applications that they intended to disseminate trial results to the participant, less than 20% (231,
 305 18.8%) specified some form of direct 'active' communication with their participants. The majority of
 306 trial teams (80.5%) left the responsibility of participants accessing trial results with the clinical care

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3 307 team or on the participant themselves. The other key finding relates to the dissemination behaviour
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5 308 reported by trial teams in their End of Study report, which demonstrated that 59.4% of completed
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7 309 trials had submitted an End of Study report compared to 20.4% that had not. However, the majority
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9 310 (74.9%) of End of Study Reports did not mention any arrangements for the provision of trial results to
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11 311 participants.

12 312
13 313 The findings from our study show the potential variability in reporting trial results back to participants
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15 314 with many trial teams not doing so, which is in line with findings from previous studies [10]. Also, the
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17 315 variability we identified with regard to how the results would be provided (i.e. paper based, web-link,
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19 316 face-to-face meeting) have also been documented in the literature [2]. However, variability of this
20
21 317 type is much less problematic (and often warranted) than that for whether the results will be offered
22
23 318 at all. It is important to consider that patients from different populations may require different modes
24
25 319 of delivery that are appropriate for their needs. The planned changes from the HRA stating they will
26
27 320 change the IRAS question from 'whether' results will be disseminated to 'when and how' is welcome
28
29 321 but research teams will still require guidance in the what, how and when of dissemination [5].

30 322
31 323 Another interesting finding is the similarity between the responses provided in the trial teams
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33 324 applications that intended to provide results to participants and those that did not. Collectively, 72%
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35 325 of the applications where trial teams stated they intended to provide results relied on either site staff
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37 326 to provide results or the participants to request the results themselves. Interestingly, these two
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39 327 categories of responses also account for nearly 70% of those applications that responded with 'No' to
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41 328 intention to disseminate results. In certain cases, an identical response was provided as justification
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43 329 for intention and no intention. For instance, 'Investigators will be informed of the study results and
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45 330 may pass on the details to participant' was a response that was observed in both the 'yes' and 'no'
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47 331 responses and in some instances was done in applications submitted by the same sponsor. This raises
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49 332 a concern that the question may be interpreted differently by different researchers and that at a
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51 333 conceptual level there is a misunderstanding about what constitutes appropriate methods of
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53 334 disseminating results. Explanatory guidance notes within the IRAS system to ensure how researchers
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55 335 are expected to operationalise and implement the dissemination of results to trial participants may
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57 336 help to resolve some of this lack of continuity.

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59 338 It is disappointing to see that 69% of the trial teams included in our audit had no intention to include
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339 the public at any stage of the research. Nearly 10% of the 850 trials deemed it inappropriate to include
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the public due to the complexity of the trial. These findings also echo results from an earlier audit of

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3 341 patient involvement in IRAS applications [11]. Particular aspects or types of research may indeed be
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5 342 difficult for a lay person to understand; however, members of the public may still be able to contribute
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7 343 to the participant enrolment or result dissemination phase [12]. A review of publicly funded trials to
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9 344 explore how PPI was included in grant applications identified that most study teams intended to have
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11 345 some form of PPI input [12]. This contrasts with the findings of this audit and others and may be reflect
12
13 346 the requirement of involvement of patients and/or the public as a condition of funding approval. This
14
15 347 raises the question as to whether there could be more linkage between funders to ensure that there
16
17 348 is consistency in research teams intentions with regards to involvement and potentially dissemination.

349

18 350 Our study highlights that most End of Study reports do not mention dissemination of results to their
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20 351 participants. However, this may not be surprising given the current guidance is not directive and states
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22 352 ', and arrangements for publication or dissemination of the research, including any feedback to
23
24 353 participants' [13]. Therefore, more explicit guidance from the Health Research Authority to include
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26 354 information on dissemination of result to trial participants in the End of Study Report should be
27
28 355 implemented. The changes planned by the HRA as part of their Transparency Agenda will require
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30 356 sponsors to submit a lay summary of the trial results and will attend to aspects of this [5]. This could
31
32 357 be strengthened by guidance on what the content of the Lay Summary should cover and mandating
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34 358 this Lay Summary as a critical requirement of trial close out

359

35 360 A recent study that surveyed teams that had published trials (involving human participants and
36
37 361 enrolling individual patients) during 2014-2015 fund only 27% of their eligible sample had
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39 362 disseminated results back to participants with a further 13% planning to do so. This study reported a
40
41 363 range of barriers the trial teams identified with regard to disseminating results and summarised these
42
43 364 as: researchers perceptions of what interests patients and what they understand; challenges reaching
44
45 365 patients; which patients to share with; need for early planning and resource; researcher motivations
46
47 366 and situational expectations; type of results to share; and, researcher specific reasons for not
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49 367 disseminating [10]. The authors propose some helpful suggestions targeting multiple players (such as
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51 368 increased scrutiny from ethics review boards, support from journals, and development of standards
52
53 369 and training) with the aim of improving practice.

370

54 371 More directive guidance, like the planned changes mentioned above, from the Health Research
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56 372 Authority is required if we plan to change researcher's behaviour with regard to disseminating results
57
58 373 of trials to those who participated. The existing guidance published in 2015 did not seem to impact
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60 374 on trial teams intentions to disseminate results (unpublished data). Therefore, the current approach

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3 375 of requiring research teams to submit a Lay Summary at the end of the study seems more appropriate.
4
5 376 It would be helpful to go one step further and request sponsor to inform the HRA when and how those
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7 377 results have been offered or disseminated to participants. The participant dissemination activity could
8
9 378 be triggered when the trial submits the End of Study report as one of the close out tasks for the team.
10
11 379 In addition, the HRA may need to take a more proactive stance with those trial teams who do not
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13 380 submit End of Study reports. Our study has shown that 20.6% of the completed trials either did not
14
15 381 submit reports or submitted incomplete data, which is not surprising given there are no consequences
16
17 382 for failing to submit.
18

19
20 383
21
22 384 In addition to the HRA, other stakeholder in the research enterprise could begin to implement systems
23
24 385 to ensure dissemination of results to trial participants becomes common place and not, at best, an
25
26 386 afterthought. For example, the BMJ pledged in 2019 that they will now ask authors of papers to
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28 387 describe their both their intentions and then evidence behaviours for dissemination of findings to
29
30 388 research participants [14].
31

32 389

33 390 **Strengths and limitations**

34
35 391 This is the first audit of ethics applications reporting trial teams' intention to disseminate results of
36
37 392 trials to those who participated. Set within a 5-year time frame we included a large sample (=1404) of
38
39 393 Phase III trials, including a range of clinical populations, interventions, comparators, outcomes, and
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41 394 supported by a range of funders. Other IRAS audits have been completed to assess registration of
42
43 395 clinical trials given a favourable opinion by UK research ethics committees, which also demonstrated
44
45 396 the value of audits of this type to assess current regulatory practice [15]. However, there were
46
47 397 limitations to our approach, principally that the IRAS data reports intention and not actual behaviour.
48
49 398 There is evidence from health psychology that intention only explain 36% of the variance in behaviour
50
51 399 and as such changing intentions does not necessarily engender behaviour change [16]. In other words,
52
53 400 the 88% of trial teams reporting they intend to disseminate results will likely be a much lower
54
55 401 proportion that actually do it. The other limitation to our study was that we relied on the identification
56
57 402 of phase of trial from trial teams. This may have introduced potential bias in teams misrepresenting
58
59 403 their trials or assumptions from our team made with regard to these trials being true pragmatic trials
60
61 404 when they may have been nearer the explanatory end of the continuum. Linked to this, it would also
62
63 405 be important to consider whether the results of our study are also true for other phases of trials.
64

65 406

66 407 **Conclusion**

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3 408 According to the HRAs IRAS system, many teams delivering Phase III trials intend to disseminate the
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5 409 results of the trial back to participants. However, reporting of whether this dissemination activity
6
7 410 actually happened is much less clear and at best happens in less than half of current Phase III trials
8
9 411 approved through IRAS. This isn't surprising given trial teams are not currently mandated to complete
10
11 412 End of Study reports and further still there are no specifications on the content of the End of Study
12
13 413 Reports or any associated Lay Summaries. There is now potential for this to change with the recent
14
15 414 publication of the HRAs transparency agenda but researchers need better guidance on what to report,
16
17 415 when and how if the benefits of dissemination are to be realised. Further research is needed to
18
19 416 conduct more embedded methodological research in these areas in order to identify best practice
20
21 417 about the what, how and when of disseminating trial result to participants.
22
23 418

24 419 **Figure 1.** IRAS applications receiving a favourable opinion between 1 January 2012 to 31 December
25 420 2017 within the UK and self-identifying as a 'Clinical Trial'.
26 421

27 422

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34 429

35 430

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37 432 HB wrote the first draft of the study protocol. KG and MZR contributed to design of the project and
38 433 development of the protocol. MZR and KG conducted data analysis. All authors (MZR, HB, KG)
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41 436

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47 442

48 443

49 444 **Competing interests**

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2
3 442 This audit forms part of a larger project that aims to develop recommendations for how to
4
5 443 appropriately feedback trial results to those who participated in them. This overarching project is
6
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11 447

12
13 448 **Patient consent for publication**

14
15 449 Not required

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18 451 **Ethics approval**

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20 452 Not required

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23 454 **Data Sharing Statement**

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25 455 Data requests should be made to the Health Research Authority.

26
27 456

28 457 **Provenance and peer review**

29
30 458 Not commissioned; externally peer reviewed

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32 459

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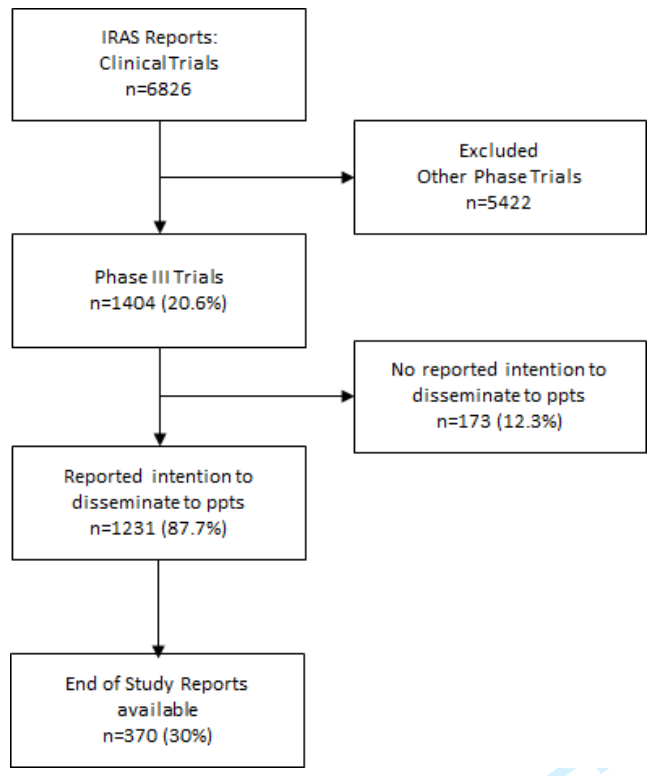
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For peer review only

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Figure 1 Summary of search results



review only

BMJ Open

Dissemination of trial results to participants in Phase III pragmatic clinical trials: an audit of trial investigators intentions.

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3 1 **Dissemination of trial results to participants in Phase III pragmatic clinical trials: an audit of trial**
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5 2 **investigators intentions.**
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9 ABSTRACT

10

11 **Objective** To determine the proportion of Phase III clinical trials given a favourable opinion by a
12 research ethics committee in the UK that provided trial results to those who participated.

13 **Design** Audit of records.

14 **Setting** Phase III clinical trials registered on the UK's research permissions system (Integrated Research
15 Application System) between the 1 January 2012 to 31 December 2017.

16 **Main outcome measures** Proportion of trial investigators that intended to provide results to trial
17 participants compared against what trials reported to ethics committees at end of study.

18 **Results** Out of 1,404 Phase III trials, 87.7% (n=1231) trials stated they intended to disseminate results
19 to participants while 12.3% (n=173) trials stated they would not. Out of these 1,231 trials, 18.8%
20 (n=231) trials intended to actively communicate trial results or a means of accessing results to their
21 participants, a further 80.5% (n=991) reported passive intention to disseminate, and for the
22 remainder (n=9) the process was unclear. Of the 370 End of Study Reports (30% of all included studies)
23 that could be accessed ten (2.7%) explicitly mentioned activities related to dissemination of findings
24 to participants with the majority (74.9%) having no mention and a further 22.4% of reports not being
25 accessible. Of the 10 which did report dissemination of results to participants the majority (n=6) were
26 through a lay summary or letter.

27 **Conclusions** Reported intention to disseminate results to trial participants amongst trial investigators
28 is high, however, reporting of feedback methods is lacking. In addition, mechanisms to ensure
29 intentions to disseminate trial results are translated into actual behaviour need to be put in place to
30 ensure those who participate in trials have the opportunity to find out about the results.

32 Article Summary

33 Strengths and limitations of this study

- 34 • First audit of the Integrated Research Application System (IRAS) to investigate trial
35 investigators reported intention to disseminate trial results to participants.
- 36 • Describes frequency of intention to disseminate and reported plans for dissemination.
- 37 • Links End of Study reports to original IRAS applications and provides a summary of overall
38 behaviours about reporting of dissemination of results in said reports.
- 39 • Linkage with End of Study Reports to report actual behaviour regarding dissemination is
40 limited due to no explicit requirement from HRA to report this activity in final report.

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3 42 Key words: *Research Transparency, Results Dissemination, Trial Conduct, Patient and Public*
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5 43 *Involvement*
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44 INTRODUCTION

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46 Clinical trials and research are increasing in the UK. In 2018, a total of 870,250 participants took part
47 in National Institute for Health Research Clinical Research Network (NIHR CRN) supported clinical
48 research studies in England alone- marking an increase of over 140,000 over the previous year [1]. The
49 cumulative cost of these studies was around £6 billion and is likely to increase as the NHS Long Term
50 Plan targets to include one million people taking part in research by 2023/24 [1]. This increase in
51 participants numbers has the potential to translate into significant improvement in delivery of
52 healthcare as long as findings are disseminated to those with responsibility to make a change (policy
53 makers) and the end users of the services (patients and health care professionals).

54 In 2008, a key review based on 28 empirical studies demonstrated that 90% of participants would
55 want to be informed of the results of the research that they were involved in [2]. Despite this interest
56 shown by participants, little is being done to provide them with results [3]. A survey on research
57 participant experience showed that 90% of respondents were happy with the information that they
58 received before or during the research. However, there was little indication that they were provided
59 with or made aware of the opportunity to access results after completion [4]. This lack of attention to
60 meeting expectations of research participants is not acceptable. When aligned with recent initiatives
61 to improve research integrity through ensuring trials are registered and that their results are published,
62 it seems an obvious next step to make sure those who participated in them (and who which without
63 they would not be possible) are informed of the results.

64

65 In order to encourage the dissemination of results, the Health Research Authority (HRA, whose core
66 purpose it 'to protect and promote the interests of patients and public in health and social care
67 research' in the UK) published guidelines, recommending that all researchers communicate results to
68 their study participants and at the very least offer the results[5].The guidelines also recommend
69 patient and public involvement (PPI) in all aspects of the research process [5]. This refers to the
70 involvement of patients and/or members of the public in the design or undertaking of the research
71 process [6]. An example of this would be patient input regarding the mode of dissemination of results
72 in order to improve the feedback process. These contributions can be very valuable as they can
73 provide an alternative perspective that the researchers may not have considered and can ensure the
74 materials are accessible to non-experts. Unlike the dissemination of results, which is not mandatory
75 for Phase III trials, the inclusion of PPI in the research process is mandated by funding bodies as a
76 prerequisite to obtaining funding.

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3 78 In the UK, applications for ethical approval are made through the Integrated Research Application
4 79 System (IRAS). The IRAS form includes questions regarding the researchers' intention to disseminate
5 80 results to participants as well as any intended PPI. Upon completion, the research team must then
6 81 submit a declaration of end of study to the research ethics committee (REC) followed by a final ethics
7 82 report within 12 months of the completion of the study (the End of Study Report). The final ethics
8 83 report should confirm any steps taken to disseminate results to participants [7]. The guidelines also
9 84 instruct researchers about the information to be included in the patient's end of study information
10 85 sheet, which should as a minimum offer the results and specify when and how participants should
11 86 expect to receive results.
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20 88 In addition, this national level guidance, there is international recognition of the ethical imperative
21 89 (specified within the Declaration of Helsinki) to offer results which is represented by the statement
22 90 '*all medical research subjects should be given the option of being informed about the general outcome*
23 91 *and results of the study*' [8].
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28 93 Whilst there is a need to provide results of any research study which a participant has contributed to,
29 94 providing results from clinical trials has salience in the current research transparency landscape [9].
30 95 Phase III clinical trials also hold a position of particular importance given all participants will have had
31 96 no choice in the treatment they received, many may not know what intervention they received,
32 97 several will have provided data through patient reported outcomes, and many are publicly funded. At
33 98 the very least, trial teams should be making the results of the studies to which these individuals
34 99 contribute to available and accessible to them in appropriate ways.
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41 101 This study aims to assess whether researchers in the UK intend to inform participants of the trial
42 102 results, plans for how results are provided, how patients are involved in this process, and finally,
43 103 whether those trial teams that intended to provide results report this activity in their end of study
44 104 reports.
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52 107 **METHODS**

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54 109 **Inclusion Criteria**

55 110 This study included all applications on the Integrated Research Application System (IRAS) during the
56 111 period 1 January 2012 to 31 December 2017 where the research team had selected filter question 2
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3 112 (defining the work as a clinical trial) and that had received a favourable Research Ethics Committee
4 113 (REC) opinion and carried out in the UK. IRAS is the UK's online system for the permissions and
5 114 approvals for health, social and community care research.
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10 116 **Data Request and Extraction**

11 117 Information regarding the IRAS form submitted by researchers was requested from the Health
12 118 Research Authority (HRA). Specific data on study descriptors such as: IRAS Project ID; REC name; REC
13 119 reference; Study title; Protocol version and date; etc was requested. In addition, data from project
14 120 relevant questions, relating to Patient and Public Involvement, plans for dissemination, and whether
15 121 participants would receive results, from within the IRAS form were requested, (see Box 1 for the
16 122 specific questions and the data types contained within them). On receipt of the data from IRAS,
17 123 additional criteria were applied to select Phase III clinical trials for inclusion (filtering to select only
18 124 those studies that reported 'Yes' to the filter 'Therapeutic confirmatory trial (Phase III)'. The rationale
19 125 for only including Phase III randomised controlled trials in this audit was due to Phase III trials largely
20 126 collecting patient reported outcomes, for which there may be more potential for demonstrable
21 127 change in practice and as such greater buy in from participants to receive the overall results from the
22 128 data collected.
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33 130 **Box 1. Requested filter questions from IRAS form**

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36 **A14-1. In which aspects of the research process have you actively involved, or will involve, patients, service users, and/or their carers, or members of the public? Give details of involvement, or if none please justify the absence of involvement.**

- 37 - Data provided: nominal data and open-ended text

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41 **A51. How do you intend to report and disseminate the results of the study?**

- 42 - Data provided: nominal data and open-ended text

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45 **A53. Will you inform participants of the results? Please give details of how you will inform participants or justify if not doing so.**

- 46 - Data provided: dichotomous data (yes/no) and open-ended text

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51 132 The data items requested from IRAS were specified in the 'HARP Software Change/Management
52 133 Information Request Form'. In addition to the data contained within IRAS we also requested access to
53 134 final ethics reports (i.e. the End of Study reports) through the HRA Assessment Review Portal (HARP)
54 135 in order to confirm a match between information provided in the IRAS form about what was planned
55 136 for feeding back results to participants with what actually happened, as reported in the final report.
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3 137 Final reports were identified by searching for specific REC reference identification numbers within
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5 138 HARP.

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8 140 **Data Analysis**

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10 141 IRAS responses which provided nominal data were summarised using descriptive statistics such as
11 142 frequencies and percentages e.g. 'Will you inform participants of the results? – Yes/No?'. Free text
12
13 143 responses were categorised using content analysis. Single level coding was applied, codes were
14
15 144 developed iteratively in discussion between team members and coding was performed by one team
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17 145 member. In order to assess the involvement of trial teams in the act of dissemination, our team
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19 146 categorised the intended means of dissemination of results as being either active or passive:

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22 148 • Active: The trial team directly informed participants of the means by which the results could
23
24 149 be accessed. For example, by a letter or by including a web link to the results.

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27 151 • Passive: Trial team did not directly inform participants of a means to access trial results. For
28
29 152 example, where the responsibility to forward the results was placed on the site team.

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31 154 **Patient and Public Involvement**

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33 155 This audit forms part of a larger project that aims to develop recommendations for researchers on
34
35 156 how to report clinical trial results appropriately to participants (RECAP: researchregistry4085). There
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37 157 are two patient partners on the Advisory group for the RECAP project who have contributed to this
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39 158 sub-study through discussion of results at team meetings. In addition, the HRA Patient and Public
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41 159 Involvement lead has also been involved in conversations about this audit and had opportunity to
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43 160 comment and guide interpretation of the results in advance of final analysis.

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45 162 **RESULTS**

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48 164 **Data Mining**

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50 165 Data on a total of 6826 trials (which had received a favourable opinion from a REC) was received in
51
52 166 the initial data set collated by the HRA based on the requested filter questions. 1404 of these were
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54 167 identified as Phase III trials as pre-specified by the trial team on the IRAS system (studies that reported
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56 168 'Yes' to the filter 'Therapeutic confirmatory trial (Phase III) – Figure 1).

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58 170 **Intention to disseminate**

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3 171 A total of 1231 (87.7%) trial teams stated they intended to disseminate results to participants while
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5 172 173 (12.3%) trials stated they would not. Researchers were then asked to provide details on how they
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7 173 intended to do so. Of those that said yes, we identified 231 (18.8%) as reporting an active effort to
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9 174 disseminate results i.e. the trial team/sponsor actively made arrangements to provide participants
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11 175 with results. The most commonly reported mode of active dissemination was directing participants to
12
13 176 a website with results (see Table 1). This was reported in 74 (32%) of trials that planned to actively
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15 177 disseminate to participants. Some trials included this at the beginning of the trial in the Participant
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17 178 Information Leaflet or at the end of participants involvement in the end of study information sheet.
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19 179 Fifty-three (22.9%) trial teams stated that they intended to provide either lay summaries or
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21 180 information sheets but did not specify any other information. Forty-four (19%) intended to send the
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23 181 results by mail directly to the participants. The 'other' category involves 4 (1.7%) trials that included
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25 182 reasons such as organising "dissemination events" and holding meetings with the participants..
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Table 1. Summary of trial team responses regarding intention to disseminate

Means of dissemination	Intention to disseminate results to participants	
	Yes	No
Active		
Provision of web link to results	74 (32%)	-
Postal letter	44 (19%)	-
Patient information sheet	37 (16%)	-
Clinic appointment	23 (10%)	-
Lay patient summary	16 (6.9%)	-
Patient choice of mode of delivery	16 (6.9%)	-
PPI group	10 (4.3%)	-
Newsletter	5 (2.2%)	-
Email	2 (0.9%)	-
Other (e.g. face-to-face meetings)	4 (1.7%)	-
<i>Total</i>	<i>231 (18.8%)</i>	
Passive		
Trial linked staff (e.g. discretion of study doctor)	549 (55.4%)	72 (41.6%)
Participant initiated request	339 (34.2%)	49 (28.3%)
Public domain (trial website)	84 (8.5%)	24 (13.9%)
Conference/scientific publication	17 (1.7%)	-
Media	1 (0.1%)	-
Public representative meeting	1 (0.1%)	-
No reason stated	-	24 (13.9%)
Other	-	4 (2.3%)
<i>Total</i>	<i>991 (80.5%)</i>	<i>173 (100%)</i>
Unclear	9 (0.7%)	
TOTAL	1231	173

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3 186 Within the trials whose teams reported an intention to disseminate results to participants, we coded
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5 187 991 as reporting a passive method to disseminate results i.e. there were no formal arrangements
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7 188 made to provide patients with access to the results. The most common method of passive
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9 189 dissemination stated the local site team, such as the study doctors or trial investigators, would provide
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11 190 results at their discretion. This accounted for 549 (55.4%) trials. Another 339 (34.2%) trial teams stated
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13 191 that results would be provided upon request but did not specify how the participants would be given
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15 192 the opportunity to request results. Finally, 84 (8.5%) intended to make the results available in the
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17 193 public domain but did not specify how the participants would be informed of or directed to these
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19 194 results.

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20 196 Responses coded as 'Unclear' (of which there were 9, 0.7%) either left the question unanswered or
21
22 197 provided a vague statement. For example, 'Participants will be informed of the results post-study.'

23 198
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25 199 A total of 173 (12.3%) trial teams reported that they did not intend to provide participants with the
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27 200 results. Of these, 72 (41.6%) stated that there were no plans to disseminate results, but that study
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29 201 investigators or study doctors may pass on the results. Forty-nine (28.3%) stated that results would
30
31 202 be provided if the participants expressed an interest or requested them. Twenty-four (13.9%)
32
33 203 provided no reason. Another 24 (13.9%) stated that results would be made available in the public
34
35 204 domain but not sent to participants directly. 'Other' (n=4, 2.3%) includes trials that mentioned the use
36
37 205 of patient groups to disseminate results or provided non-specific statements such as 'Patients will be
38
39 206 informed about the results of their study in an individual manner'.

40 207 41 208 42 209 **Patient and Public Involvement**

43 210 We also wanted to determine whether those trials that planned to disseminate results to trial
44
45 211 participants were better overall at including patients in the design and conduct of the trial. Therefore,
46
47 212 we analysed whether and how the trial teams that intended to disseminate results included patients
48
49 213 as partners in their studies.

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51 215 Within the sample of 1231 who planned to disseminate results to participants, 381 (31%) trial teams
52
53 216 also reported they intended to involve patients or the public in the design or conduct of their trial.
54
55 217 The largest proportion of PPI was observed in the dissemination phase with 227 trials accounting for
56
57 218 59.6% while only 4.5% (n= 17) of trial teams proposed input during the analysis phase. Elsewhere, 180
58
59 219 (47.2%) reported they would incorporate PPI in the design phase of the research; 123 (32.3%) would
60
220 seek input whilst the undertaking of the trial; and 121 (31.7%) proposed to involve patients or public

221 in the management phase (see Table 2). It is important to note that involvement was not mutually
 222 exclusive to one individual design or conduct category and researchers could select involvement
 223 across multiple categories.

224

225 **Table 2. Researcher reported Patient Public Involvement in trial design and/or conduct**

Aspect of trial	IRAS reported PPI in design and/or conduct of trial			
	Intention to disseminate results to ppts (n=381)		No intention to participate results to participants (n=42)	
	Frequency	%	Frequency	%
Design	180	47.2	16	38.1
Management	121	31.7	6	14.3
Undertaking	123	32.3	28	66.7
Analysis	17	4.5	2	4.8
Dissemination	227	59.6	11	26.2

226 *Totals for % are greater than 100 as categories are not mutually exclusive and research teams could report PPI
 227 across several aspects of the research.

228

229 Forty-two (24%) of the 173 trial teams that had no intention of disseminating results back to
 230 participants did report patient or public involvement in at least one aspect of the trial process. Within
 231 this sample of 42, undertaking the research was reported most frequently as involving PPI (n=28,
 232 66.6%), followed by design (n=16, 38%), dissemination (n=11, 26%), management (n=6, 14.3%), and
 233 analysis (n=2, 4.7%). Again, it is important to note that involvement was not mutually exclusive to one
 234 category.

235

236 A total of 850 (69%), from the 1231 trial teams that intended to disseminate result to participants,
 237 stated they would not be involving PPI partners at any stage of the research process. Among these,
 238 244 (28.7%) deemed PPI to be unnecessary due to the sufficient expertise present among the
 239 members of the research team or other sources e.g. 'It was felt that sufficient input had been gained
 240 from other sources.'. A further 213 (25.0%) trials responded that it was inappropriate to involve
 241 members of the public due to the complex or experimental nature of the trial or the use of an
 242 unlicensed drug. One hundred and forty-five (16.6%) trials stated that all aspects of the research
 243 process were sole responsibility of the trial sponsor. One hundred and five (12.4%) trials did not
 244 provide an explanation for not doing so. 'Other' involved 34 (3.9%) trials that do not give a specific
 245 reason for the lack of PPI or simply describe the details of the trial itself. For example. 'No patients,
 246 services and/or their carers, or members of the public were involved with the design of the protocol'.
 247 Finally, 'Prescribed design' accounted for 12 (1.4%) of the responses, which refers to studies that are
 248 using previously implemented trial designs and who deemed PPI not necessary. Responses are
 249 summarised in Table 3.

250

251 **Table 3. Summary of responses to justification of no patient public involvement**

Reason	Frequency (n)	% of total
Sufficient Expertise	244	28.7
Sponsor Responsibility	145	17.1
Inappropriate – Experimental nature of trial	110	12.9
Unanswered	105	12.4
Inappropriate – complexity of trial	83	9.8
Commercial trial	82	9.6
Inappropriate – unprescribed drug	20	2.4
Confidentiality	15	1.8
Prescribed Research Design	12	1.4
Other	34	3.9
TOTALS	850	100

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253

254 **End of Study Report**

255 Data for the 1231 trial teams that intended to disseminate results was extracted from HARP to identify,
 256 firstly, whether these studies submitted an End of Study report. A large proportion of trials (517 (42%))
 257 were still in progress when the data was requested while 90 trials (7.3%) had been terminated or
 258 abandoned and as such no End of Study reports were available for these trials. Of the 624 completed
 259 trials, 370 (59.3% of completed trials and 30% total sample) submitted a final ethics report, while 127
 260 (20.4% of completed trials and 10.3% of total sample) failed to do so and 127 (20.4% of completed
 261 trials and 10.3% of total sample) had incomplete data registered within the HARP system making
 262 analysis difficult. (Table 4).

263 **Table 4. End of Study Report Status**

Report Status	Frequency (n)	% of total	
Completed trials	Submitted	370	30.0
	Not submitted	127	10.3
	Incomplete HARP data ²	127	10.3
Trial in progress ¹	517	42.0	
Trial terminated/abandoned	90	7.3	
TOTAL	1231	100	

274 ¹Trial in progress: trial currently recruiting or in follow up, or, not yet started, or, trial complete and not
 275 reported but has up to 12 months to report.

276 ²Incomplete HARP data: HARP has trial registered but is incomplete. e.g. does not clearly state that trial ever
 277 started/little or no documentation uploaded to HARP.

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281 Of the 370 studies that did submit an End of Study report, the majority of the trial teams (277, 74.9%)

282 did not mention any arrangements made regarding the dissemination of trial results back to

283 participants yet all expressed intention to do so on the original IRAS application. Six studies (1.6%)
 284 provided a copy of the lay summary or referred to it in the report or the cover letter. Evidence of other
 285 strategies used to inform participants of the trial results were also poorly represented with 2 (0.5%)
 286 studies providing the patient end of study sheet, 1(0.3%) offering a final follow up visit, and another
 287 1 (0.3%) mentioning presentation at a scientific conference. Whilst indicating the End of Study Reports
 288 had been uploaded, the reports of 83 (22.4%) trials were inaccessible due to some requiring
 289 passwords or email access or yet to be uploaded by the REC to the HARP system. Therefore, details
 290 from these reports could not be extracted or included in the analysis See Table 5.

291

292 **Table 5. Reporting of dissemination of result to trial participants in End of Study reports**

293

Dissemination of results reported	2013	2014	2015	2016	2017	2018	2019	TOTAL (n/%)
No mention	1	23	42	58	65	53	35	277 (74.9)
Confirmation of Lay summary/letter ¹	-	-	-	-	1	3	2	6 (1.6)
Patient end of study sheet attached	-	-	-	-	-	1	1	2 (0.5)
Follow up visit	-	-	-	-	-	-	1	1 (0.3)
Presentation at scientific conference	-	-	1	-	-	-	-	1 (0.3)
Report inaccessible ²	5	3	7	3	16	32	17	83 (22.4)
TOTAL	6	26	50	61	82	89	56	370 (100)

294 ¹ Confirmation of lay summary/letter either as an attached copy or mentioned in final report/cover letter.295 ² Report inaccessible: Reports that require password/email access or have to be uploaded by the REC.

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297

298 **DISCUSSION**

299

300 **Key findings**

301 This study reports the first audit of researcher intentions and self-reported behaviours with regard to
 302 dissemination of clinical trial results to participants across the UK using reports within the HRA
 303 regulatory system. We have found that while the majority (1231, 87.7%) of trial teams stated in their
 304 applications that they intended to disseminate trial results to the participant, less than 20% (231,
 305 18.8%) specified some form of direct 'active' communication with their participants. The majority of
 306 trial teams (80.5%) left the responsibility of participants accessing trial results with the clinical care

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3 307 team or on the participant themselves. The other key finding relates to the dissemination behaviour
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5 308 reported by trial teams in their End of Study report, which demonstrated that 59.4% of completed
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7 309 trials had submitted an End of Study report compared to 20.4% that had not. However, the majority
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9 310 (74.9%) of End of Study Reports did not mention any arrangements for the provision of trial results to
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11 311 participants.

12 312
13 313 The findings from our study show the potential variability in reporting trial results back to participants
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15 314 with many trial teams not doing so, which is in line with findings from previous studies [10]. Also, the
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17 315 variability we identified with regard to how the results would be provided (i.e. paper based, web-link,
18
19 316 face-to-face meeting) have also been documented in the literature [2]. However, variability of this
20
21 317 type is much less problematic (and often warranted) than that for whether the results will be offered
22
23 318 at all. It is important to consider that patients from different populations may require different modes
24
25 319 of delivery that are appropriate for their needs. The planned changes from the HRA stating they will
26
27 320 change the IRAS question from 'whether' results will be disseminated to 'when and how' is welcome
28
29 321 but research teams will still require guidance in the what, how and when of dissemination [5].

30 322
31 323 Another interesting finding is the similarity between the responses provided in the trial teams
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33 324 applications that intended to provide results to participants and those that did not. Collectively, 72%
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35 325 of the applications where trial teams stated they intended to provide results relied on either site staff
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37 326 to provide results or the participants to request the results themselves. Interestingly, these two
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39 327 categories of responses also account for nearly 70% of those applications that responded with 'No' to
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41 328 intention to disseminate results. In certain cases, an identical response was provided as justification
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43 329 for intention and no intention. For instance, 'Investigators will be informed of the study results and
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45 330 may pass on the details to participant' was a response that was observed in both the 'yes' and 'no'
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47 331 responses and in some instances was done in applications submitted by the same sponsor. This raises
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49 332 a concern that the question may be interpreted differently by different researchers and that at a
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51 333 conceptual level there is a misunderstanding about what constitutes appropriate methods of
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53 334 disseminating results. Explanatory guidance notes within the IRAS system to ensure how researchers
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55 335 are expected to operationalise and implement the dissemination of results to trial participants may
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57 336 help to resolve some of this lack of continuity.

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59 338 It is disappointing to see that 69% of the trial teams included in our audit had no intention to include
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339 the public at any stage of the research. Nearly 10% of the 850 trials deemed it inappropriate to include
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the public due to the complexity of the trial. These findings also echo results from an earlier audit of

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3 341 patient involvement in IRAS applications [11]. Particular aspects or types of research may indeed be
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5 342 difficult for a lay person to understand; however, members of the public may still be able to contribute
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7 343 to the participant enrolment or result dissemination phase [12]. A review of publicly funded trials to
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9 344 explore how PPI was included in grant applications identified that most study teams intended to have
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11 345 some form of PPI input [12]. This contrasts with the findings of this audit and others and may be reflect
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13 346 the requirement of involvement of patients and/or the public as a condition of funding approval. This
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15 347 raises the question as to whether there could be more linkage between funders to ensure that there
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17 348 is consistency in research teams intentions with regards to involvement and potentially dissemination.

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20 350 Our study highlights that most End of Study reports do not mention dissemination of results to their
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22 351 participants. However, this may not be surprising given the current guidance is not directive and states
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24 352 ', and arrangements for publication or dissemination of the research, including any feedback to
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26 353 participants' [13]. Therefore, more explicit guidance from the Health Research Authority to include
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28 354 information on dissemination of result to trial participants in the End of Study Report should be
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30 355 implemented. The changes planned by the HRA as part of their Transparency Agenda will require
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32 356 sponsors to submit a lay summary of the trial results and will attend to aspects of this [5]. This could
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34 357 be strengthened by guidance on what the content of the Lay Summary should cover and mandating
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36 358 this Lay Summary as a critical requirement of trial close out

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39 360 A recent study that surveyed teams that had published trials (involving human participants and
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41 361 enrolling individual patients) during 2014-2015 fund only 27% of their eligible sample had
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43 362 disseminated results back to participants with a further 13% planning to do so. This study reported a
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45 363 range of barriers the trial teams identified with regard to disseminating results and summarised these
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47 364 as: researchers perceptions of what interests patients and what they understand; challenges reaching
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49 365 patients; which patients to share with; need for early planning and resource; researcher motivations
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51 366 and situational expectations; type of results to share; and, researcher specific reasons for not
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53 367 disseminating [10]. The authors propose some helpful suggestions targeting multiple players (such as
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55 368 increased scrutiny from ethics review boards, support from journals, and development of standards
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57 369 and training) with the aim of improving practice.

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60 371 More directive guidance, like the planned changes mentioned above, from the Health Research
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373 Authority is required if we plan to change researcher's behaviour with regard to disseminating results
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of trials to those who participated. The existing guidance published in 2015 does not seem to have
impacted on trial teams intentions to disseminate results . Therefore, the current approach of

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3 375 requiring research teams to submit a Lay Summary at the end of the study seems more appropriate.
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5 376 It would be helpful to go one step further and request sponsor to inform the HRA when and how those
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7 377 results have been offered or disseminated to participants. The participant dissemination activity could
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9 378 be triggered when the trial submits the End of Study report as one of the close out tasks for the team.
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11 379 In addition, the HRA may need to take a more proactive stance with those trial teams who do not
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13 380 submit End of Study reports. Our study has shown that 20.6% of the completed trials either did not
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15 381 submit reports or submitted incomplete data, which is not surprising given there are no consequences
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17 382 for failing to submit.

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19 383
20 384 In addition to the HRA, other stakeholder in the research enterprise could begin to implement systems
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22 385 to ensure dissemination of results to trial participants becomes common place and not, at best, an
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24 386 afterthought. For example, the BMJ pledged in 2019 that they will now ask authors of papers to
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26 387 describe how and when they plan to disseminate findings to research participants [14].
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29 389 **Strengths and limitations**

30 390 This is the first audit of ethics applications reporting trial teams' intention to disseminate results of
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32 391 trials to those who participated. Set within a 5-year time frame we included a large sample (=1404) of
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34 392 Phase III trials, including a range of clinical populations, interventions, comparators, outcomes, and
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36 393 supported by a range of funders. Other IRAS audits have been completed to assess registration of
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38 394 clinical trials given a favourable opinion by UK research ethics committees, which also demonstrated
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40 395 the value of audits of this type to assess current regulatory practice [15]. However, there were
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42 396 limitations to our approach, principally that the IRAS data reports intention and not actual behaviour.
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44 397 There is evidence from health psychology that intention only explain 36% of the variance in behaviour
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46 398 and as such changing intentions does not necessarily engender behaviour change [16]. In other words,
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48 399 the 88% of trial teams reporting they intend to disseminate results will likely be a much lower
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50 400 proportion that actually do it. The other limitation to our study was that we relied on the identification
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52 401 of phase of trial from trial teams. This may have introduced potential bias in teams misrepresenting
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54 402 their trials or assumptions from our team made with regard to these trials being true pragmatic trials
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56 403 when they may have been nearer the explanatory end of the continuum. Linked to this, it would also
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58 404 be important to consider whether the results of our study are also true for other phases of trials.
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61 406 **Conclusion**

62 407 According to the HRAs IRAS system, many teams delivering Phase III trials intend to disseminate the
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64 408 results of the trial back to participants. However, reporting of whether this dissemination activity

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3 409 actually happened is much less clear and at best happens in less than half of current Phase III trials
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5 410 approved through IRAS. This isn't surprising given trial teams are not currently mandated to complete
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7 411 End of Study reports and further still there are no specifications on the content of the End of Study
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9 412 Reports or any associated Lay Summaries. There is now potential for this to change with the recent
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11 413 publication of the HRAs transparency agenda but researchers need better guidance on what to report,
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13 414 when and how if the benefits of dissemination are to be realised. Further research is needed to
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15 415 conduct more embedded methodological research in these areas in order to identify best practice
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17 416 about the what, how and when of disseminating trial result to participants.
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18 418 **Figure 1.** Summary of search results.
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28 428

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30 430 HB wrote the first draft of the study protocol. KG and MZR contributed to design of the project and
31 431 development of the protocol. MZR and KG conducted data analysis. All authors (MZR, HB, KG)
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39 439

40 440 **Competing interests**

41 441 This audit forms part of a larger project that aims to develop recommendations for how to
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3 443 RECAP: researchregistry4085). KG was supported by an MRC Methodology Research Fellowship
4
5 444 (MR/L01193X/1).

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8 446 **Patient consent for publication**

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10 447 Not required

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13 449 **Ethics approval**

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15 450 Not required

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18 452 **Data Sharing Statement**

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20 453 Data requests should be made to the Health Research Authority.

21 454

22
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24
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28 458 **ORCID iDs**

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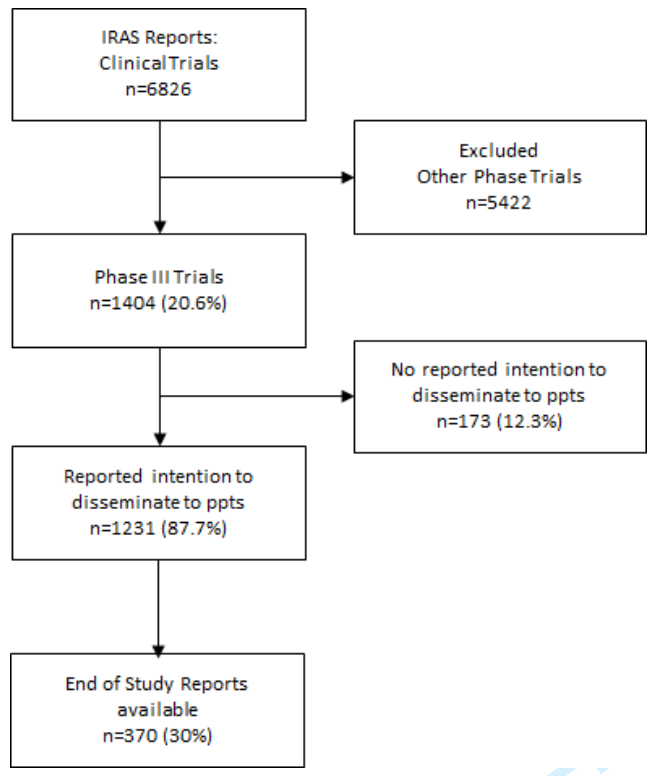
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For peer review only

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Figure 1 Summary of search results



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