Chapter 8 Use of monetary incentives to boost participant questionnaire response rates in the eTHoS study: the 'to incentivise or not to incentivise' studies

Introduction

Response rates to the questionnaires administered at follow-up in the eTHoS study were routinely monitored at monthly in-house team meetings. Although response rates to the two early questionnaires were acceptable, there was no further contact with participants until the 12-month follow-up questionnaire and no contact between the 12- and 24-month questionnaires. The response rate to the 12-month follow-up questionnaire was observed to be lower than expected part way through the recruitment period. Options to improve the response rates were therefore considered by the study team. Literature reviews looking at methods to increase response rates were reviewed, and it was found that monetary incentives were likely to increase response rates.[56] However, there was limited evidence from studies in the UK and RCTs. It was therefore decided to conduct a formal evaluation of whether or not using a monetary incentive improved the response rate. This study was called 'to incentivise or not to incentivise' (IONTI). Surprisingly, the response rates continued to be low, and a need to protect the response rates in the main study was paramount; hence, the IONTI study was stopped early after 15 months. Subsequently, after a further review of the literature, a second incentive approach was implemented and its impact was assessed in the IONTI-2 study. The background, design and findings from both of these 'studies within a trial' (SWATs) are described in this chapter. *Appendix 4* gives an overview of the timeline for both the IONTI and IONTI-2 studies.

'To incentivise or not to incentivise'

In early 2013, the response rates to the 12-month follow-up questionnaire were found to be lower than expected at 69% (97/140 as of 25 February 2013); the expected response rate was 85%. Following discussion at the PMG meeting on 26 March 2013, it was decided that action needed to be taken in order to increase the response rate as much as possible. In order to choose the most effective intervention to increase the follow-up response rates in the eTHoS study, the team turned to the literature. A review published by The Cochrane Library[56] evaluating strategies to boost response rates looked at 110 different strategies in 481 trials using postal questionnaires and 27 different strategies in 32 trials using electronic questionnaires. Although the eTHoS study follow-up data were collected using self-report by postal and electronic means, the largest proportion of responses were postal and, therefore, this mode of administration was also prioritised when designing the SWAT.

The literature review showed that in postal but not electronic questionnaire studies, monetary incentives were suggested to be the most likely to be effective in increasing response rates (OR 1.87, 95% CI 1.73 to 2.04), although there was significant heterogeneity among results.[56] The amount of the incentive might also affect the impact of monetary incentives. The review showed that in the 37 studies included, in which larger and smaller monetary incentives were compared, larger amounts were more effective. A further variation in studies using monetary incentives is whether the incentive is conditional or unconditional, that is, whether or not a voucher can be forwarded on the condition that the participant returns a completed questionnaire, or the voucher can be sent with the questionnaire to be completed and the participant does not have to do anything before receiving it. The review found that unconditional monetary incentives were more effective than conditional monetary incentives. However, very few studies used gift vouchers, few were clinical trials and only a small number were carried out in the UK; therefore, the generalisability of the findings could be questioned.

One study carried out, in the UK, by Gates *et al.*[57] showed a positive impact on response rates following the introduction of a monetary incentive, a £5 gift voucher, into their RCT on advice for whiplash patients. Participants ($n = 2144$) were randomised to two groups: one group received a gift voucher at both follow-up points and the other group did not receive any incentive. Participants in the former group ($n = 1070$) received the gift voucher unconditionally with their questionnaire at the 4- and 8-month follow-up points. The results showed that the incentive group was more likely to return the questionnaires (relative risk 1.10, 95% CI 1.05 to 1.16), an absolute increase of 7% of questionnaires returned. However, the authors acknowledged that further research was needed in order to establish whether or not the findings were generalisable to different populations and different types of trials.

In addition, the eTHoS study also presented an opportunity to assess the introduction of an incentive part way through a study to address the lower than anticipated response rate to a postal questionnaire; this is a scenario that triallists regularly face. Further steps were also taken in order to protect the response rate of the main study during the IONTI study; however, these were not randomised.

Based on the limited evidence available, the eTHoS study team decided to conduct a SWAT looking at the impact of an unconditional and, therefore, small £5 high-street gift voucher on questionnaire response rates at the 12- and 24-month follow-up points, and whether or not the timing of the incentive has an impact. The specific research questions are explored in detail in the following sections.

Aim

The overall aim was to assess whether or not sending an unconditional £5 high-street gift voucher improves the response rate to the 12- and 24-month patient questionnaires.

The specific research questions were as follows.

1. Does sending an unconditional £5 high-street gift voucher with the 12-month follow-up questionnaire improve the response rate to this questionnaire?
2. Does sending an unconditional £5 high-street gift voucher with the 24-month follow-up questionnaire improve the response rate to this questionnaire?
3. Is there any indication of an interaction when a £5 high-street gift voucher is sent at 12 and 24 months?

Methods: 'to incentivise or not to incentivise'

Participants/eligibility

As of 5 June 2013, patients enrolled in the eTHoS study, across all clinical sites, who had yet to receive their 12-and 24-month follow-up questionnaires, were randomised into one of four groups described in *Table 52*.

TABLE 52 Description of the four participant groups in the IONTI study

	Group			
Follow-up time point	1	2	3	4
12-month follow-up	Voucher	Voucher	No voucher	No voucher
24-month follow-up	No voucher	Voucher	Voucher	No voucher

Materials

All participants who were randomised to receive a voucher were sent a covering letter describing the purpose of the 12- or 24-month follow-up questionnaire and why a voucher was included (see *Appendix 4*).

The IONTI study participants received the same standard 12- and 24-month follow-up questionnaires as described in *Chapter 3*, and the same reminders (postal then telephone reminders).

A £5 Love2Shop (Park Group plc, London, UK) voucher was included with the postal questionnaire according to group allocation. This brand of vouchers was chosen as they would be accepted in a range of high-street shops across the UK and should therefore be convenient to use for all participants.

Randomisation

Simple randomisation (1 : 1 : 1 : 1) was completed to allocate the eTHoS study participants to one of the four groups.

NHS research ethics and other permissions

Ethics approval was sought for the IONTI study and submitted as a substantial amendment to the main study. Ethics approval was received on 25 April 2013 for amendment 16 of the REC reference number 10/S0802/17.

Sites also had to approve the IONTI study. Sites were informed about the IONTI study as standard practice for all substantial amendments and had 35 days of submission to object to the amendment, otherwise approval would be assumed.

One of the co-sponsors (University of Aberdeen) required a statement regarding the possible tax implications to be included in the IONTI study questionnaire cover letters. This was included as of June 2013. However, this was removed in April 2014, as the sponsor reviewed its guidelines for this statement to be applicable only to amounts exceeding £10.

Primary outcomes

The primary outcome was the response rates at 12 and 24 months for the four groups.

In addition, through the routine study management system, the following information was collected: date questionnaire sent, if a reminder was sent and date sent, if a second reminder was sent and date sent, if a response was received along with mode utilised (postal or online) and date of receipt.

Statistical analysis

The response rates to questionnaires at 12 and 24 months between the incentive and the non-incentive groups were compared using logistic regression. Two separate analyses were carried out, one each for the return of the 12- and 24-month questionnaires. For the analysis of return of the 12-month questionnaire, only a 12-month incentive main effect was included. The analysis of return of the 24-month questionnaire included both a 12-month and a 24-month incentive main effect. The possibility of an interaction was explored using an additional incentive at 12 months by incentive at 24-month interaction effect. Models were adjusted for the minimisation variables (sex, baseline EQ-5D-3L score, haemorrhoid grade and centre) and 95% CIs are reported.

In addition, a non-randomised comparison of the impact of the IONTI study on the response rates was completed. This was also analysed using logistic regression with the IONTI study viewed as a single intervention (ignoring each individual's randomised allocation) with the pre- and post-IONTI study responses compared.

Estimated sample size

A total of 600 participants were anticipated to be recruited or still to have 12-month questionnaires sent by 1 May 2013, and could potentially have been included in the IONTI study subject to approval and implementation. A sample of 300 per group would have allowed a difference of 10% (70–80%) to be detected with 80% statistical power at the two-sided 5% significance level. Seventy per cent was the estimated proportion, as of February 2013, of participants returning their 12-month questionnaire. The 24-month level was uncertain, given the low numbers that had reached that time point.

Stopping rules

If the monetary incentive was found to be effective, the IONTI study would be stopped and all participants due a 12- or 24-month follow-up questionnaire would receive a voucher. The possibility of the IONTI study being detrimental was not considered and a date for interim analysis was not set.

Study within a trial registration

The SWAT was registered on the SWAT repository store held by the Northern Ireland hub for Trials Methodology Research [this was referenced as SWAT13 Jonathan Cook (2013 February 01 1237)].

Other initiatives taken to improve response rates in the main study

As of September 2013, the effectiveness of the reminders was reviewed by the study team. Telephone reminders for 12 and 24 months were found to be ineffective and expensive. For this reason, the second reminder was changed to a postal reminder.

As of December 2013, both reminders for the 12- and 24-month questionnaires were shortened to contain only the primary outcome measure (EQ-5D-3L). The second shortened reminder (EQ-5D-3L) was also introduced at this time to replace telephone call reminders, and was to be sent at 18 months, replacing the participant travel cost questionnaire, which was now postponed to be sent after the 24-month follow-up questionnaire at 27 months.

As of May 2014, a newsletter was sent to participants 1 week before their 12- or 24-month follow-up questionnaires, highlighting that they would soon, approximately 1 week later, receive their next follow-up questionnaire. Participants who had completed their follow-up received a version of the newsletter without a pre-notification.

Results

Two sites did not approve the amendment for the IONTI study and, therefore, participants from 27 sites were eligible and randomised in the IONTI study. One site objected because of the possibility that participants' confidentiality might be breached as the sponsor is legally required to share details of individuals who have received payments if requested by HM Revenue & Customs, whereas the other site objected on ethical grounds.

In addition, one participant who was randomised to receive the voucher returned it, as he felt that as he did not receive surgical treatment, he was not eligible to receive the voucher.

Flow of participants

Figure 24 shows the flow of participants who were included in the IONTI study. There were 142 participants randomised to group 1 (voucher at 12 months but not at 24 months); 124 participants randomised to group 2 (voucher at 12 and 24 months); 123 randomised to group 3 (no voucher at 12 months but voucher at 24 months); and 132 participants randomised to group 4 (no voucher at 12 or 24 months). In total, 25 participants withdrew by the end of the study and one had died (unrelated). Baseline data are shown in *Table 53*.

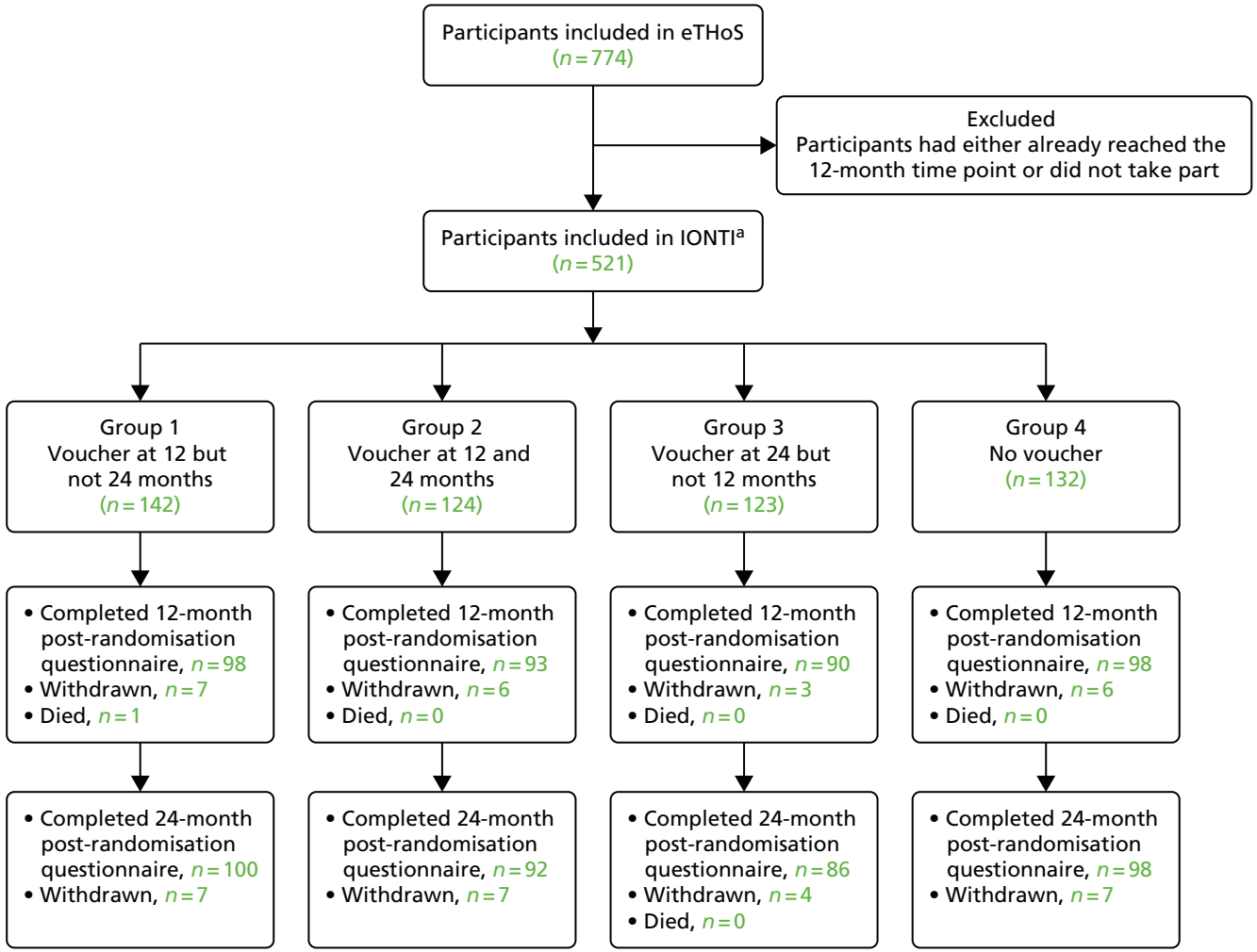

FIGURE 24 Flow of participants in the IONTI study. a, Participants eligible while the IONTI study was running from June 2013 until it was stopped in October 2014. Withdrawal refers to withdrawal from main study.

TABLE 53 Baseline characteristics for participants in the IONTI study

Characteristic	Trial arm			
	No voucher (*N* = 132)	12 months only (*N* = 142)	24 months only (*N* = 123)	Both time points (*N* = 124)
Age (years), *n*, median (IQR)	132, 50 (40–59)	142, 48 (38–58)	123, 50 (41–60)	124, 50 (42–61)
Sex (male), *n* (%)	62 (47.0)	73 (51.4)	64 (52.0)	63 (50.8)
BMI, *n*, mean (SD)	127, 26.8 (4.9)	137, 27.7 (5.2)	121, 26.6 (5.0)	120, 27.1 (5.3)
Grade of haemorrhoid, *n* (%)				
II	27 (20.5)	37 (26.1)	27 (22.0)	26 (21.0)
III	85 (64.4)	83 (58.5)	81 (65.9)	78 (62.9)
IV	20 (15.2)	22 (15.5)	15 (12.2)	20 (16.1)
Previous haemorrhoid surgery, *n* (%)	37 (28.0)	52 (36.6)	45 (36.6)	31 (25.0)
Comorbidities, *n* (%)	1 (0.8)	–	2 (1.6)	2 (1.6)
Systemic medications, *n* (%)				
Aspirin	7 (5.3)	1 (0.7)	7 (5.7)	7 (5.6)
Warfarin	2 (1.5)	1 (0.7)	1 (0.8)	1 (0.8)
Clopidogrel	2 (1.5)	1 (0.7)	4 (3.3)	2 (1.6)
Steroids	–	2 (1.4)	1 (0.8)	–
Other	3 (2.3)	–	1 (0.8)	1 (0.8)
Pain (VAS), *n*, mean (SD)	131, 2.6 (2.4)	140, 3.0 (2.5)	121, 2.4 (2.7)	121, 2.8 (2.9)
Analgesia, *n* (%)				
Yes	42 (31.8)	44 (31.0)	40 (32.5)	37 (29.8)
Missing	1 (0.8)	1 (0.7)	3 (2.4)	2 (1.6)
Number of days in a week with analgesia, *n*, mean (SD)	42, 3.8 (2.0)	44, 4.3 (2.2)	40, 5.1 (2.2)	36, 4.4 (2.1)
EQ-5D-3L, *n*, mean (SD)	132, 0.812 (0.216)	142, 0.735 (0.264)	123, 0.771 (0.262)	124, 0.751 (0.266)
SF-36, *n*, mean (SD)				
Physical component summary	130, 49.6 (9.3)	139, 48.5 (9.5)	119, 48.3 (10.0)	124, 48.3 (10.4)
Mental component summary	130, 50.4 (10.1)	139, 49.1 (11.1)	119, 50.2 (11.7)	124, 47.9 (12.3)
CIS, *n*, mean (SD)	129, 3.9 (3.6)	137, 4.5 (3.7)	118, 3.4 (3.7)	120, 4.6 (4.5)
HSS, *n*, mean (SD)	129, 12.9 (3.7)	134, 12.5 (3.9)	116, 12.5 (3.7)	120, 12.5 (4.3)
Patient reporting tenesmus, *n* (%)				
Always	2 (1.5)	6 (4.2)	4 (3.3)	3 (2.4)
Often	18 (13.6)	18 (12.7)	14 (11.4)	14 (11.3)
Sometimes	36 (27.3)	36 (25.4)	33 (26.8)	28 (22.6)
Rarely	19 (14.4)	30 (21.1)	17 (13.8)	19 (15.3)
Never	57 (43.2)	51 (35.9)	50 (40.7)	60 (48.4)
Missing	–	1 (0.7)	5 (4.1)	–

TABLE 53 Baseline characteristics for participants in the IONTI study (*continued*)

Characteristic	Trial arm			
	No voucher ($N = 132$)	12 months only ($N = 142$)	24 months only ($N = 123$)	Both time points ($N = 124$)
Patient preference, *n* (%)				
Strongly prefer better short-term recovery	11 (8.3)	12 (8.5)	11 (8.9)	10 (8.1)
Prefer better short-term recovery	11 (8.3)	11 (7.7)	6 (4.9)	3 (2.4)
No preference	42 (31.8)	57 (40.1)	51 (41.5)	47 (37.9)
Prefer lower risk of recurrence	33 (25.0)	38 (26.8)	28 (22.8)	28 (22.6)
Strongly prefer lower risk recurrence	35 (26.5)	23 (16.2)	24 (19.5)	34 (27.4)
Missing	–	1 (0.7)	3 (2.4)	2 (1.6)

BMI, body mass index.

In general, the groups were well balanced. *Table 54* provides the IONTI study response rate results. There were no statistically significant differences between the groups at 12 or 24 months. Similarly, there was no evidence of an interaction effect (*Tables 55* and *56*).

TABLE 54 The IONTI study: responses to questionnaires at 12 and 24 months

Response time point	Time point of voucher, *n* (%)			
	12 months		24 months	
	No	Yes	No	Yes
Response at 12 months				
No	62 (24.3)	69 (25.9)	–	–
Yes	193 (75.7)	197 (74.1)	–	–
Response at 24 months				
No	71 (27.8)	74 (27.8)	76 (27.7)	69 (27.9)
Yes	184 (72.2)	192 (72.2)	198 (72.3)	178 (72.1)

TABLE 55 The IONTI study: ORs of responses to questionnaires at 12 and 24 months

Response time point	OR (95% CI)	*p*-value
Response at 12 months		
Voucher at 12 months	0.99 (0.72 to 1.37)	0.962
Response at 24 months		
Voucher at 12 months	0.93 (0.60 to 1.44)	0.760
Voucher at 24 months	0.85 (0.48 to 1.52)	0.586
Interaction	1.39 (0.69 to 2.79)	0.358

TABLE 56 The IONTI study: before-and-after analysis to response to questionnaires at 12 and 24 months

Time point post randomisation	Responded to questionnaire, *n* (%)		OR (95% CI)	*p*-value
	Yes	No		
12 months				
Before	178 (72.1)	69 (27.9)	–	–
After	408 (77.4)	119 (22.6)	1.31 (0.84 to 2.04)	0.237
24 months				
Before	30 (71.4)	12 (28.6)	–	–
After	532 (72.7)	200 (27.3)	1.01 (0.55 to 1.86)	0.980

The 'to incentivise or not to incentivise'-2 study

Response rates remained lower, at 75% (375/498) for the 12-month questionnaire and 60% (127/212) for the 24-month questionnaire, than the expected rate of 85%, despite the fact that the IONTI study ran for 1 year. The eTHoS study team turned to the literature again for guidance.

A systematic literature review suggested that higher-value incentives were effective in increasing response rates to postal questionnaires in randomised trials. In their review, Brueton *et al.*[58] looked at randomised SWATs that compared strategies with increase response rates to follow-up questionnaires in RCTs. They identified 38 eligible SWATs, of which 14 tested incentives and two compared size of incentive. The two trials ($n = 902$) showed that those receiving a higher-value incentive were more likely to respond to questionnaires than those who received lower-value incentives (relative risk 1.12, 95% CI 1.04 to 1.22; $p < 0.005$), irrespective of how the incentive was delivered.

Based on the evidence reviewed above, the study team decided to conduct another monetary incentive study, IONTI-2. In the IONTI-2 study a high-value gift voucher (£30) was sent to participants who returned a fully completed 12- or 24-month questionnaire or associated reminders. A fully completed questionnaire was defined as one in which the primary outcome measure, the EQ-5D-3L, was completed.

Aim

The aim of the IONTI-2 study was to investigate the impact of a conditional £30 gift voucher on response rates at the 12- and 24-month follow-up points.

Methods: the 'to incentivise or not to incentivise'-2 study

Participants/eligibility

As of 17 October 2014, patients enrolled in the eTHoS study across all clinical sites, who had yet to receive their 1-year and/or 2-year follow-up questionnaire, were eligible.

Materials

All participants received a covering letter describing the purpose of the 12- or 24-month follow-up questionnaire and were informed that on return of a completed questionnaire they would receive a £30 gift voucher as a token of appreciation for their time spent completing the questionnaire (see *Appendix 4*).

The IONTI-2 participants received the same standard 12- and 24-month follow-up questionnaires as described in *Chapter 3*, and the same reminders (by this time amended to two postal reminders containing only the EQ-5D-3L, and an 18-month reminder if no return at 12 months).

On receipt of a completed questionnaire (12- or 24-month questionnaire reminders or 18-month reminder), the primary outcome measure had to be completed, a £30 gift voucher was triggered and sent to the participant.

The Love2Shop brand of vouchers was chosen as these would be accepted in a range of high-street shops across the UK and should therefore be convenient to use for all participants.

As of 21 January 2015 a label was added to the front of questionnaires, giving participants a choice to opt out from receiving the gift voucher (see *Appendix 4*). The team felt that this option should be made available for participants who were taking part in the study solely for altruistic reasons.

NHS research ethics and other permissions

Ethics approval was sought for the IONTI-2 study and a substantial amendment was submitted to the main study. Ethics approval was received on 8 September 2014 for amendment 27 for REC reference number 10/S0802/17.

Sites also had to approve the IONTI-2 study. Sites were informed about the IONTI-2 study as standard practice for all substantial amendments and could object within 35 days of submission of the amendment, otherwise approval would be assumed.

As vouchers had a value of more than £10, the sponsor required a statement regarding the possible tax implications to be included with the vouchers. A compliment slip was included in the mailing with the voucher informing participants of possible tax implications (see *Appendix 4*).

Primary outcomes

The main primary outcome was response rates at 12 and 24 months for participants included in the IONTI-2 study.

In addition, through the routine study management system, the following information was collected: date questionnaire was sent, if a reminder was sent and date sent, if a second reminder was sent and date sent, if a response was received along with mode utilised (postal or online) and date of receipt.

Statistical analysis

The primary analysis was a before-and-after analysis of the impact of the £30 gift voucher at 12 and/or 24 months using logistic regression with adjustment for the minimisation variables. The primary analysis included all participants who had not already reached the 12- and/or 24-month time point.

A further analysis using the preceding IONTI study period data along with all of the data up to the end of the 24-month follow-up period was carried out.

A post hoc sensitivity analysis was carried out as a result of the overlapping influence of the IONTI study. For the 12-month analysis, this included participants not included in the IONTI-2 study, participants who were randomised to no voucher and those who received the voucher at 24 months only. For the 24-month analysis, this included participants not included in the IONTI-2 study and participants who were randomised to receive no vouchers in the IONTI-2 study. Data on responses were collected and compared.

One interim analysis for futility was planned once the outcome for 75% of the anticipated participants in the IONTI-2 study was known at 24 months. Based on this, it was decided to continue the study to completion.

Owing to a system error, the shortened reminders (introduced in December 2013) were not issued to participants at 24 months for a period of 12 months during the IONTI study. This might have impacted on the response rate at 24 months. To protect the host study, eTHoS, these missed 24-month reminders were sent out during the IONTI-2 study and these included the conditional voucher incentive to maximise response rates. These returned reminders were not included in the final analysis for the IONTI-2 study.

Estimated sample size

A total of 440 recruits were anticipated to still be due to receive their 24-month questionnaires at the time of design. Based on a simple pre–post comparison of the return rate, a sample of 216 per group would allow a difference of 16% (60–75%) to be detected with 90% statistical power at the two-sided 5% significance level. This may be reduced slightly because of the single interim analysis, although it is anticipated to be over 80%.

Study within a trial registration

The SWAT was registered on the SWAT repository store held by the Northern Ireland hub for Trials Methodology Research [reference: SWAT13 Jonathan Cook (2013 February 01 1237)].

Other initiatives taken to improve the response rates in the main study

No new steps were taken during the IONTI-2 study.

Results

'To incentivise or not to incentivise'-2

All sites agreed to take part in the IONTI-2 study. The IONTI-2 study began on 17 October 2014 when the IONTI study ceased. A total of 5% of participants (24/481) who completed the questionnaire opted not to receive the voucher. *Table 57* provides the IONTI-2 study results, which showed no statistical evidence of a change in the response rate.

Owing to the different follow-up points that individuals were at in that point in time, a small proportion of participants took part in both SWATs – 'a middle group'. *Table 58* provides the IONTI-2 sensitivity analyses results, exploring this 'middle group'. There was no evidence of a difference in the 12-month response rates after the incentive was given. This was also the same at 24 months, but there was a slight increase in response rates (71.4% before the incentive, 75.9% after the incentive).

TABLE 57 The IONTI-2 study: full dataset

	Responded to questionnaire, *n* (%)			
Time point post randomisation	Yes	No	OR (95% CI)	*p*-value
12 months				
Before	443 (75.1)	147 (24.9)	–	–
After	143 (77.7)	41 (22.3)	1.13 (0.75 to 1.69)	0.559
24 months				
Before	205 (69.3)	91 (30.7)	–	–
After	357 (74.7)	121 (25.3)	1.31 (0.97 to 1.76)	0.074

TABLE 58 The IONTI-2 study: sensitivity analysis

Time point post randomisation	Responded to questionnaire, *n* (%)		OR (95% CI)	*p*-value
	Yes	No		
12 months				
Before	434 (77.1)	129 (22.9)	–	–
After	143 (77.7)	41 (22.3)	1.01 (0.66 to 1.55)	0.974
24 months				
Before	205 (71.4)	82 (28.6)	–	–
After	349 (75.9)	111 (24.1)	1.25 (0.87 to 1.80)	0.230

Discussion

Findings from the IONTI and IONTI-2 studies were inconclusive with regard to the overall question. The IONTI study was stopped early as a result of concerns that it was having a negative impact on retention, based on anecdotal information and interim results. The overall response rates for the main study (eTHoS) were prioritised over the value of continuing the IONTI study. Findings from the IONTI study were statistically inconclusive. The overall analysis of IONTI-2 was similarly inconclusive, including the sensitivity analysis, which might be viewed as the purer analysis (excluding the group that had received an incentive in the IONTI study), which also showed no difference in response rate at 12 months. The 24-month finding was also statistically significant, but there was a slightly higher post-incentive response rate in both analyses.

As both SWATs were found not to be effective, the cost of these incentives per participant has not been calculated.

Taken together, the findings were, at best, inconclusive, and, from the study team's perspective, clearly disappointing. No positive effect was observed and there was the suspicion and possibility of a negative impact, despite previous work evaluating incentives as being very favourable.[56,58] It is possible, however, that the negative finding here was only a chance finding. Alternatively, they could reflect something specific to the study and the way in which the incentives were delivered. There are a number of possible contributing factors. Of particular note was the requirement of the sponsor to include a statement in the covering letter regarding possible tax implications in the IONTI study. Anecdotal feedback from participants suggested that this caused concern to some participants. This institutional judgement was later revised on appeal, and the cover letter used was modified accordingly most of the way through the IONTI study intervention period. The eTHoS study participants received multiple questionnaires early in the follow-up period with a number of similar outcomes, which may have resulted in lower response rates. Introducing a relatively low-value incentive at 12 or 24 months might be viewed as too little and/or too late. It was later hoped that the study team could carry out qualitative research to fully explore the cause of the negative impact. This was not followed through, because of the substantial regulatory barriers and lack of resources. Further research in this area is recommended, preferably in a variety of settings to allow disease- and population-specific cohorts, along with features of follow-up, to be explored.

Multiple strategies to improve recruitment and response rate are regularly used in multicentre trials in which recruitment and/or response rates are lower than hoped. Often these are used without much evidence to support their use. It was the investigators' expectation at the initiation of the IONTI study that the use of incentives could be only positive (or, at worst, that they would have no impact). The findings from the IONTI studies question this assumption and points to the need for care when introducing new interventions part way through a study. Bower *et al.*[59] suggested that SWATs or 'nested' trials are needed to test the

effectiveness of retention strategies. However, triallists should be aware of the challenges of implementing SWATs part way through pragmatic trials. As noted by others in Glidewell *et al.*;[60] 'Interventions to increase response rates may incur negative consequences' contrary to the intuitive expectation.

Both studies had a number of limitations in terms of the evaluation of an intervention. A confounding factor during the conduct of the IONTI study was the use of pre-notification newsletters, which were also employed as a method to boost retention. There is some limited evidence that these are beneficial to boosting response rates.[56] Newsletters were issued 1 week prior to the 12- and 24-month questionnaire being distributed across all IONTI study groups; as such, it was not possible to untangle what impact this would have had upon the overall study. The IONTI and IONTI-2 studies were carried out in a fully 'open' manner, with the interim results monitored as part of the routine study management process by the study team. This reflected their primary aim to address the lower-than-anticipated response rate, with the main study being the priority. The decision to stop the study was not according to a prespecified stopping rule, but a corporate judgement of the study team. As such, this monitoring process increased the possibility of a misleading finding.

The IONTI-2 study had a number of limitations. As a before-and-after study, its findings are susceptible to secular trends and other concurrent changes. In particular, some participants were involved in both studies, 'a middle group', which makes the interpretation more difficult. We carried out a sensitivity analysis that excluded this group; however, such exclusion of data is not without its own risks in terms of bias. More generally, recruitment to trials often has ebb and flows during the life cycle of a trial for various reasons, and this could have led to some bias being included in the comparison.

Participants in the IONTI-2 study were given an 'opt-out' option when receiving the £30 voucher. This was taken up by a small proportion [5% (24/481)] of participants, but the true 'opt-out' level may include some who did not respond.

Summary

The IONTI studies did not find any evidence in favour of the use of incentives to increase the response rate, and there was some suggestion of a negative impact. There are a number of contextual aspects that may explain this unexpected finding. Care is needed when introducing a new intervention into an ongoing study. Future evaluations of incentives are needed to explore the impact of contextual issues that may moderate their impact.