11 Appendices

Appendix 1 - The influence of patient support group delivered research awareness strategies on research recruitment and retention (PURPOSE Study)

Background

Recruitment and retention rates in clinical trials can be low and many patients, who are keen to be involved in clinical trials cannot participate because they do not know about the research opportunities available to them. Patients are keen to ensure that clinical trials are delivered quickly so that clinical research questions can be answered and are generally supportive of research. Patient support groups are often keen to promote and support research.

APF is the leading national UK pulmonary fibrosis charity. It supports patient support groups, gives patients a voice, raise awareness of pulmonary fibrosis and supports research. There are currently 77 pulmonary fibrosis patient support groups in the UK and all NHS Trusts in England with specialist centres, and most of the main ILD hospitals in the other three nations, involved with TIPAL have an affiliated support group. ILD patient support groups generally meet every two months (fortnightly to quarterly), with interim mailing of newsletters, and groups are attended by between 20 and 60 patients or relatives.

This SWAT aims to assess the influence of patient support group research awareness and support strategies on clinical trial recruitment and retention.

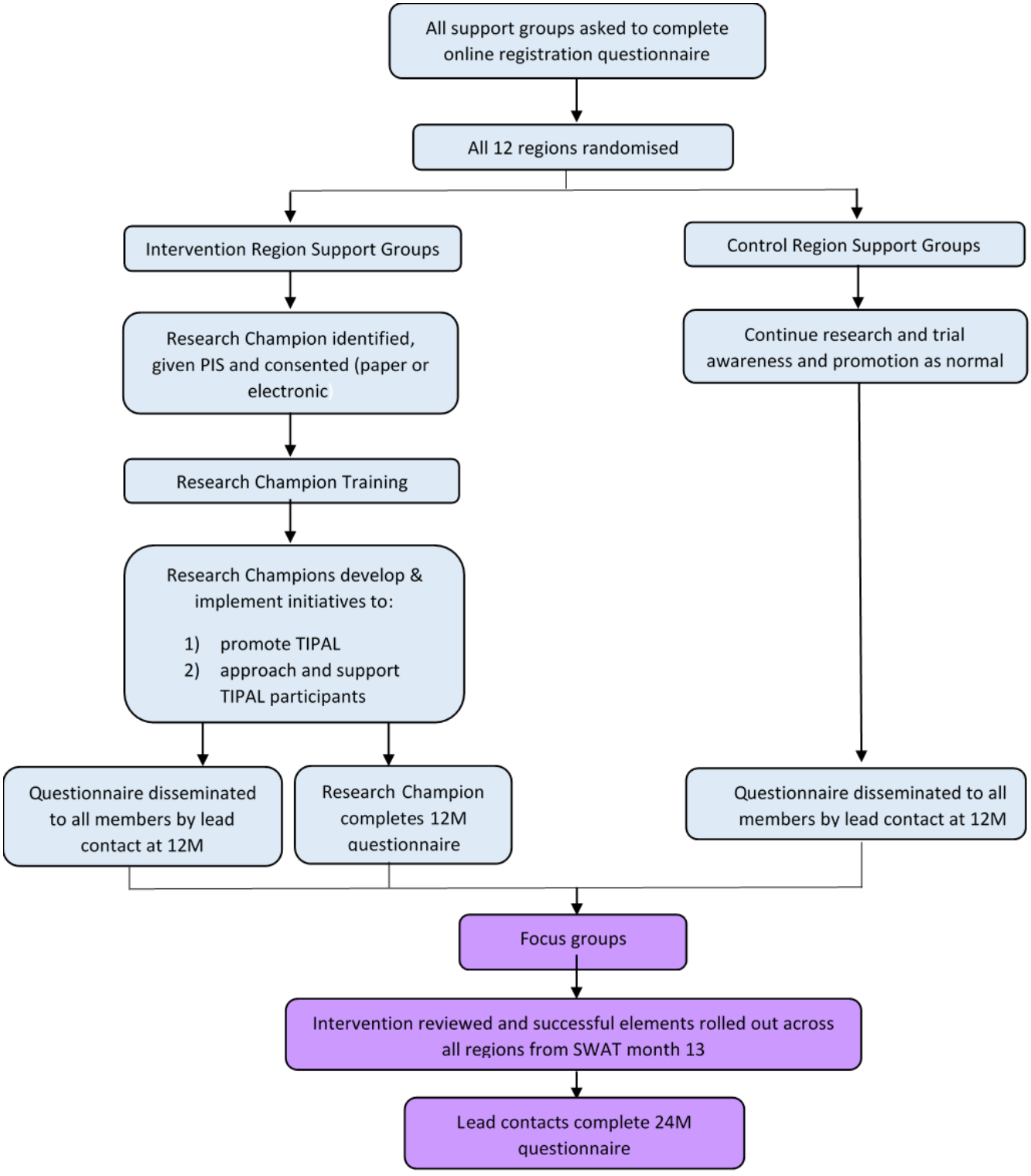
Methods

This will be a cluster-randomised SWAT of enhanced patient support group engagement with assessment of research activity captured by screening logs and questionnaires. Clustering will occur at regional level to reduce contamination between support groups which cover one or more NHS Trust participating in the TIPAL Trial. A list of APF support groups and TIPAL sites by region is available from APF and the TIPAL trial manager respectively.

The following regions will be randomised to either the PURPOSE intervention or control arm:

- London
- South East England
- South West England
- East Midlands
- West Midlands
- East of England
- North East England
- North West England
- Yorkshire and Humberside
- Wales
- Scotland
- Northern Ireland

Figure 4 PURPOSE study flowchart



Blue = Phase 1
Purple = Phase 2

Cluster randomisation will be stratified by the approximate number of support group members from each region from a pre-randomised list generated by the study statistician prior recruitment commencing in the main trial. This will be calculated from the PURPOSE Registration Questionnaire

completed by the lead contact of each support group prior to the start of the study. The NCTU research team or APF Research Champion Lead will confirm arm allocation by email to all the APF support groups as soon as possible after the randomisation of their region (cluster unit).

Participants - clusters

Regions will only be included in the study if:

1. At least one TIPAL site has opened or is expected to open to recruitment in the region within 6 months of the start of the study.
2. Interest has been confirmed by at least one of the regional APF support groups within the region.

All APF support groups affiliated with NHS Trusts participating in the TIPAL trial are eligible to participate and will be invited. The support group leads will be asked to confirm an interest in taking part by signing (electronically or wet ink) and returning a copy of a PURPOSE Study registration questionnaire sent by NCTU/APF. This document will detail the requirements of the PURPOSE study with further details provided in the APF PURPOSE support group information leaflet. The study registration questionnaire will also record support group membership size, name a lead contact for the PURPOSE study, describe the ways the group communicates with its members and list typical subjects discussed at meetings or sent out as part of newsletters. All support groups will be asked to complete the study registration questionnaire prior to the intervention period. Completion is optional and consent is inferred by virtue of completion.

The PURPOSE study will not impact the usual role, function or activity of the patient support groups; groups in intervention regions will implement initiatives in addition to their usual remit and control groups will continue to operate as usual in the first 12 months of the study.

Intervention

Within regions randomised to the intervention arm, the lead contact at each support group will be asked to identify a local Research Champion(s) who will lead the TIPAL trial research awareness campaign.

Champions may be patients or a patient's carer, friend or relative. Research champions may act as a regional research champion supporting multiple support groups within the same region where the region is randomised to the intervention arm and individual support groups are unable to identify a research champion. Groups and/or regions may identify more than one Research Champion and/or a Deputy Research Champion to allow adequate support and/or continuation of the intervention where circumstances/availability change. Champions will be provided with a study information sheet and be asked to sign a written consent form if they are willing to take on the role prior to intervention delivery. Consent forms may be completed on paper or electronically following a study consultation in person or remotely (via video/phone call) with a member of the APF research team. Where electronic forms are completed, participants will need to verbally consent to providing their email address to receive the consent form and wet-ink equivalent signatures will be recorded. A research champion recruitment log will be maintained centrally.

The intervention will consist of the following steps:

1. Recruitment of at least one volunteer research champion.
2. Training of the champions/champion teams.
3. Development and implementation of initiatives to promote the TIPAL study within the APF support group.
4. Development and implementation of initiatives to approach and support their members who are participating in the TIPAL trial.

Guidance regarding initiatives will be provided to champions in a non-prescriptive way to allow each APF support group to tailor them to their group specificities. Initiatives will most likely encompass activities such as discussion about research within the group, providing generic and study-specific information about the TIPAL study, writing and disseminating newsletters.

The APF Research Champion Lead will facilitate regular meetings (online or in-person) as an opportunity for research champions to collaborate and discuss initiatives as a closed, dedicated platform.

Support groups randomised to the intervention arm in the first 12 months are referred to as phase 1 groups in the participant/support group facing documents.

Control

Within regions randomised to the control arm, APF Support Groups will not undertake any formal method for enhancement of recruitment through the support groups, although local PIs are able to discuss research with those groups as standard practice. All patients will have access to the twitter feeds and generic information on the APF website and TIPAL webpage. Support group correspondence and communication will continue as normal.

The control groups will have access to the intervention materials and training at the end of the 12-months evaluation period for implementation from then onwards. Informed consent will be obtained from lead contacts prior to them completing APF led training in the delivery of the initiatives to increase research awareness within the support group. Therefore both groups will deliver the successful initiatives from month 13 onwards; this is referred to as phase 2 in the participant/support group facing documents. Demographic patient support group data relating to the control groups during phase 1 will be collected retrospectively from phase 2 lead contacts by a questionnaire (electronic or paper completion).

Primary outcomes

The following outcomes will be assessed at 12 months from the start of the study:

- The difference between the number of trial participants recruited from control and intervention patient support groups, as obtained from the TIPAL screening log.
- The difference between the numbers of withdrawn trial participants from control and intervention patient support groups, as obtained from the TIPAL screening log and eCRF.

The following exploratory outcomes will also be assessed:

- The difference in overall recruitment within regions allocated to control and intervention.
- The difference in the overall number of withdrawn TIPAL participants.

- The number of self-reported self-referrals or enquiries to participate in the TIPAL study as obtained from the TIPAL trial screening log and support group member questionnaire
- The difference in the completeness of primary endpoint between participants from control and intervention APF support groups, as obtained from the TIPAL eCRF.
- The difference in hits on the TIPAL webpage from control and intervention regions from data analytics provided by the webpage host.
- The perceived change in APF support group members' general knowledge and enthusiasm about research as measured by a support group member questionnaire sent to all members of all APF support group involved in the PURPOSE study.
- A description of the interventions undertaken, as obtained from a study-specific questionnaire completed by research champions/lead contacts at 12 months (intervention regions only) and 24 months.
- An appraisal of the intervention by a series of focus groups facilitated by a member of APF or another appropriate individual at 12 months

Data Collection Methods

Figure 4 outlines PURPOSE data collection.

Data on the primary outcome measures and data on self-referrals will be obtained from the linked-anonymised TIPAL screening log and eCRF.

During screening for the TIPAL trial, patients will be asked whether they are members of an APF Support group and, if so, the name of the group and whether they self-referred to the TIPAL trial (meaning they approached their clinical team to enquire about the trial). TIPAL participants will be asked their 'support group status' at the 12 month follow-up visit.

This linked-anonymised data will be collected by TIPAL sites on the TIPAL screening log and used to assess the difference between the overall number of trial participants recruited from control and intervention patient support groups. It will also be used to compare the rates of self-referral from control and intervention patient support groups.

The screening data will also be used to compare withdrawal data, obtained from the TIPAL eCRF withdrawal form to assess the difference between the overall numbers of withdrawn trial participants from control and intervention patient support groups.

Research Champions will be asked to complete a study-specific non-validated online questionnaire at 12 months and 24 months. The questionnaire link will be sent via email by APF and/or the NCTU team at the relevant timepoints. Alternatively, questionnaire responses may be provided on paper where preferred. In this instance, APF will facilitate entry into the electronic questionnaire system, performing ad hoc quality checks for transcription accuracy. The questionnaire responses will be reviewed and discussed by a review group comprising members of APF and other members of the TIPAL team and will be used to refine the intervention.

Data completeness of the primary endpoint of TIPAL participants, linked to a support group within. an intervention region, will be compared with those in control regions at 12 and 24 months from the start of the study.

At 12 months, a non-validated study-specific questionnaire will be distributed to control and intervention support group research champions/lead contacts for electronic dissemination to all support group members, to assess members' general knowledge and enthusiasm about research and confirm the number of self-reported self-referrals or enquiries about the TIPAL study. Alternatively, questionnaire responses may be provided on paper where preferred. In this instance, APF will facilitate entry into the electronic questionnaire system, performing ad hoc quality checks for transcription accuracy. To supplement this, TIPAL participants will be asked if they are willing to complete the NIHR Participant in Research Experience Survey (PRES) questionnaire at the end of their participation as part of the standard delivery programme conducted by the Clinical Research Network. Participants will be asked to record the name of their patient support group (if applicable) on the PRES questionnaire.

Routine web analytics data of traffic on the main TIPAL webpage will be collected throughout the trial. The webpage host will provide a report based on data exported from Google Analytics including the number of and location of webpage hits on the TIPAL webpage. This will be exported at the end of the trial and will enable a comparison between the traffic from control and intervention regions.

Data captured on the TIPAL eCRF and questionnaire data will be kept securely on the UEA servers (in a SWAT specific office 365 folder). This data will be only accessible to members of the TIPAL trial team at NCTU, and external regulators if requested.

Focus groups will be facilitated by APF at 12 months to allow feedback and discussions with support groups to appraise the interventions put in place. It is anticipated that 3 - 4 focus groups will occur, either online or in-person, with approximately 3 to 5 participants, including: a research-engaged support group, a less research-engaged support group and research champions (may be split into two groups to ensure effective discussions are feasible with the number of attendees). Level of research engagement will be subjectively assessed by APF based upon performance in Phase 1. Focus groups will be conducted online and facilitated either by APF or an independent qualitative researcher. Discussions will be recorded using the inbuilt recording feature will be used meaning that audio and video is recorded. Focus group meetings will take approximately 60 - 90 minutes and participants must consent to participate prior to the discussions taking place. Participation in focus groups is voluntary and does not affect participation in the rest of the PURPOSE study or TIPAL trial (if applicable). Focus group participants will be assigned a PID upon consent in order for a linked-anonymised transcript to be produced from each discussion. Consent may be documented electronically (with a wet-ink equivalent signature) or on paper. Only the PURPOSE study team will be able to link the participants to their PID. Discussions will follow the meeting structure outlined in the PURPOSE focus group topic guide.

PURPOSE study data including focus group recordings will be stored securely for 25 years by NCTU.

Analysis

The analysis will be based on the intention-to-treat principle but as this is a cluster trial, a mixed model will be used with a random effect for the clustering variable of 'region'. For the outcome measures that are count data, a Poisson mixed model will be used. For the outcome of number of participants recruited, the model will adjust for the membership size of each APF support group at baseline (provided by APF). The choice of offset is to control for the different self-referrals from support groups in the study, the assumption being that the recruitment rate should depend on the size of the support

groups, with large support groups having larger numbers of self-referrals. For the outcome of the number of participants withdrawn, the model will adjust for the number of participants randomised at each APF support group.

A descriptive analysis will be undertaken to compare the number of self-reported self-referrals or enquiries to participate in research studies from participants, the number of patients recruited via patient support groups and the number of hits on the study webpage. We will also compare the completeness of the primary endpoint data at each site and the results from a questionnaire to assess general knowledge and enthusiasm about research as well as the degree of empowerment and motives for participating in research, plus adverse or unintended consequences.

The number of recruited participants per site: The analysis will be based on a random effects Poisson regression model with site included as a random effect and an offset of the size of the site.

Primary outcome completeness: The analysis will be based on a random effect logistic regression model with site included as a random effect.

Focus group transcripts: Thematic analysis of all transcripts will be conducted by an experienced individual affiliated with UEA, identified by the TIPAL trial team.

Further information will be contained in a study specific Statistical Analysis Plan which will be finalised prior to the end of the study.