TITLE OF THE PROTOCOL:

Group-based positive psychotherapy for people living with Acquired Brain Injury: A feasibility study

Short title/Acronym: PP4ABI

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ISRCTN ID: **To be assigned**

STUDY SUMMARY/SYNOPSIS

TITLE	**Group-based positive psychotherapy for people living with Acquired Brain Injury: A feasibility study**
SHORT TITLE	PP4ABI
Protocol Version Number and Date	Version 2 [16th April 2020]
Methodology	Randomised controlled trial
Study Duration	24 months in total – 7 months to recruit and follow up the intervention group meetings
Study Centre	• Swansea Bay University Health Board (SBUHB) • Cardiff and Vale University Health Board (CVUHB) • Hywel Dda University Health Board (HDUHB)
Aim	To undertake a feasibility study as a first step towards conducting a full-scale randomised-controlled trial (RCT) to determine the clinical and cost effectiveness of this novel intervention for people living with ABI compared to a 'treatment as usual' control group (TAU).
Number of Subjects/Patients	60 (20 per arm)
Main Inclusion Criteria	- Confirmed diagnosis of ABI - Ability to actively engage in the intervention as determined by their neuropsychological assessment scores and their clinician - Living in the community - Psychological distress - Age eighteen years or older - Living within the catchment area of one of the participating health boards - At least three-month post injury at the point of recruitment allowing time for spontaneous recovery and for the person to become aware of their difficulties and the implications of this on their lives
Statistical Methodology and Analysis	The primary outcome regarding feasibility will be assessed against the ACCEPT criteria for the trial. A Qualitative Data Analysis Plan will document how the data will be managed, analysed and reported. Thematic analysis will be used to explore key themes/codes that emerge from the data. . Quantitative data analysis will focus on descriptive statistics and feasibility outcomes. While clinical effectiveness will not be formally evaluated at this stage, we will inspect quantitative data for early evidence that the intervention shows promise or, conversely, appears unlikely to result in the desired outcome We will also test the feasibility of collecting data required for a full economic evaluation in a future trial.

Protocol Agreement Page

The clinical study as detailed within this research protocol **(Version 2.0, dated 1st April 2020)**, or any subsequent amendments will be conducted in accordance with the Research Governance Framework for Health & Social Care (2005), the World Medical Association Declaration of Helsinki (1996) and the current applicable regulatory requirements and any subsequent amendments of the appropriate regulations.

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1 Glossary of Terms and Abbreviations

ABI	Acquired Brain Injury
AE	Adverse Event
AR	Adverse Reaction
ASR	Annual Safety Report
CI	Chief Investigator
CRF	Case Report Form
CVUHB	Cardiff and Vale University Health Board
DASS	Depression, Anxiety and Stress Scale
DMC	Data Monitoring Committee
HDUHB	Hywel Dda University Health Board
ICF	Informed Consent Form
ISRCTN	International Standard Randomised Controlled Trial Number
MIS	Mentor Information Sheet
NHS R&D	National Health Service Research & Development
Participant	An individual who takes part in a clinical trial
PI	Principle Investigator
PIS	Participant Information Sheet
PP	Positive Psychology
PPT	Positive Psychotherapy
QDAP	Qualitative Data Analysis Plan
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SBUHB	Swansea Bay University Health Board
SDV	Source Document Verification
SOP	Standard Operating Procedure
TMG	Trial Management Group
TAU	Treatment as usual (i.e. the control group)
TBI	Traumatic Brain Injury
TSC	Trial Steering Committee

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2 Introduction

Acquired brain injury (ABI) leads to an array of emotional, behavioural, physical and cognitive impairments, which can have a profound impact on psychological wellbeing. Estimates of prevalence for depression following brain injury range from 27-64% (Glenn et al., 2001; Jorge et al., 2004; Osborn et al., 2014) and a further 20% experience high levels of anxiety (Campbell Burton et al., 2013). Critically, the psychological consequences of ABI are generally hidden and are associated with poor involvement in rehabilitation, hospital re-admission, long-term disability, limited social activity, reduced ability to manage physical conditions, increased health service usage, suicide and a general increase in risk for mortality (Naylor et al., 2012; Ayerbe et al., 2013; van Eeden et al., 2016; Gillen et al., 2001). People affected by ABI – as with other chronic conditions – have little access to psycho-social interventions to address ongoing holistic needs: almost three- quarters of people living with ABI feel that their psychological needs are not met (McKevitt et al., 2011; Oyesanya, 2017).

Evidence supports the efficacy of positive psychological interventions in a healthy population and across a host of diseases, disorders and conditions (Bolier et al., 2013). Within the ABI population, group and one-to-one positive psychotherapy (PPT) have been reported to increase happiness (Andrewes et al., 2014; Cullen et al., 2016) and reduce symptoms of anxiety (Cullen et al., 2016). Both studies reported that the feasibility and effectiveness of PPT in people living with ABI is promising.

Our study differs from this preliminary research in several important ways:

1. our intervention is broader in scope, drawing on positive psychology as well as wellbeing science including a focus on the individual, others and the wider environment;
2. we make use of service user mentors who have been trained to co-deliver the intervention, providing a meaningful role for mentors and hope and inspiration for participants attending the group;
3. we include physiological measures of wellbeing which may offer insight into the links between mental distress and physical health;
4. we include teaching about 'positive health behaviours' and behavioural change, which has shown to be an important determinant of wellbeing;
5. we incorporate qualitative as well as health economic components in line with recommendations on planning feasibility studies (Gannon, 2017; O'Cathain et al., 2014).

Why is this research needed: This research is needed because our NHS is under unprecedented strain, in part because of the increasing number of people living with chronic conditions. The typical model of health care, 'the acute medical model' was designed to treat acute conditions. Chronic conditions have now replaced acute conditions as leading burdens of morbidity, mortality, and health care expenditure. However, models of healthcare have not adapted to reflect this. Our work paves the way for new more effective and sustainable models of healthcare, for people with ABI and potentially other chronic conditions. Moreover, when we asked our service users what they needed from their community health services following their brain injuries the message was clear: they wanted opportunities for a meaningful and purposeful life.

This work has the potential to a) reduce psychological distress; b) increase wellbeing; c) reduce barriers to rehabilitation; d) prevent further neuropsychological impairment; e) embed and embody the principles of co-production and partnership working in the healthcare sector, and f) lay a platform for a more effective and sustainable model of healthcare for those living with chronic conditions in Wales.

Theoretical Framework: A systematic meta-analysis (Bolier et al., 2013) on the effectiveness of positive psychology interventions including PPT concluded that such interventions are effective in the enhancement of wellbeing and also help to reduce psychological distress. Only two studies have explored the impact of PPT on people living with ABI and these two pilot/feasibility studies have reported promising findings (Cullen et al. 2018; Andrewes et al. 2014). Recently an evidenced based manualised PPT programme was published by Rashid and Seligman (2018). It was influenced by Seligman's model of wellbeing (2012), characterised by PERMA. PERMA is an acronym that describes the five components thought to be essential for the experience of wellbeing: Positive emotion, Engagement, Relationships, Meaning and Achievement. Our proposed intervention makes use of some of the techniques in this manual. However, our intervention is broader in scope, drawing on wellbeing science as well as PPT. Our own theoretical models of

health and wellbeing - GENIAL 1.0 and GENIAL 2.0 (Kemp, Fisher & Arias, 2017; Mead et al., unpublished, respectively) demonstrate the importance of 'health behaviours' in pathways to health and wellbeing as well as 'social connections' and 'positive psychological experiences'. The PERMA model and techniques from PPT map onto the 'social connections' and 'positive psychological experiences' identified in the GENIAL model. However, PPT typically does not include strategies to increase positive health behaviours, which our model shows are a critical component of wellbeing. Accordingly, our intervention emphasises the importance of positive health behaviours on mental health, such as physical activity (Chekroud et al., 2018), a diet rich in fruit and vegetables (Jacka et al., 2017), a good night's sleep (Baglioni et al., 2011), smoking cessation (Taylor et al., 2014) and avoiding excess consumption of alcohol (Tembo, Burns & Kalembo, 2017). GENIAL refers to the impact of Gene – Environment interactions on the functioning of the vagus Nerve, which is critical for effective social Interactions (Porges, 2011) and plays an important regulatory role over allostasis (Tracey, 2002), subsequently either increasing risk for premature mortality, or promoting Longevity (Hillebrand et al., 2013). Our GENIAL model predicts that the vagus nerve plays a critical regulatory role of multi-systemic, downstream pathways that can lead to either premature mortality or longevity. Vagal nerve functioning can be enhanced by the experience of a) positive psychological moments; b) positive social ties; and c) positive health behaviours, which subsequently facilitates individual pathways to health and wellbeing (Kemp, Arias, & Fisher, 2017a; Kemp, Koenig, & Thayer, 2017b). Our model therefore predicts that our intervention may impact vagal function to have a beneficial effect on physical and mental health – something we wish to explore in a large-scale RCT by measuring Heart Rate Variability (an index of vagal functioning). Finally, our intervention has been developed considering three fundamental contributors to wellbeing: the individual, which has typically been target of positive psychology and PPT; relationships with others, the focus on which is gaining traction in the field of health psychology (e.g. Haslam et al., 2017) and the environment, which includes community, socio-cultural factors such as poverty and social cohesion (Bandura, 2004) as well as considerations relating to the challenges that we now face as a species, including climate change and the wellbeing of future generations (e.g. Lindstrøm & Eriksson, 2010). Guided by this work our intervention helps participants think about ways in which they can achieve a sense of meaning by connecting with others and their community/environment.

3 Trial Objectives and Design

3.1 Trial Objectives

Aims: To undertake a feasibility study as a first step towards conducting a full-scale randomised-controlled trial (RCT) to determine the clinical and cost effectiveness of this novel intervention for people living with ABI compared to a 'treatment as usual' control group (TAU).

Objectives: Our objectives for the planned study are to monitor the aspects of the study to determine feasibility with respect to the following categories outlined in the standardised ACCEPT checklist (Charlesworth et al., 2013). This includes recruitment, compliance with intervention, randomisation and blinding, data collection and analysis procedures, research governance and trial management. The criteria to be used are shown in the table below and we will use a pass/fail system to determine whether the trial has passed each criterion.

Criteria	FAIL	PASS
Recruitment across sites	Issues at 1+ sites	All 3 sites recruit eligible patients
Recruitment rate (%)	<50%	≥ 50%
Intervention compliance (%) - clinicians	<80%	≥ 90%
Intervention compliance (%) - participants	<70%	≥ 70%
Randomisation process (inc. predictions)	2+ issues with randomising	<2 issues randomising participants
Data collection from participants	<70%	≥ 70%
Attrition rates	≥ 30%	<30%
Difference between groups in SAEs	≥ 30%	<30%

In addition to monitoring feasibility against the ACCEPT checklist we will also use qualitative methods to offer insight into the specific objectives of the study design. For example, patients experience of recruitment, eligibility, consent and their experience of several aspects of the intervention (session context, length, homework, their experience of using

the materials. The outcome of this monitoring would be to make amendments where necessary in order to progress to a full-scale trial.

3.2 Trial Design

Randomised controlled trial allocating eligible patients to either the treatment (positive psychology [PP] intervention) or control (treatment as usual) at a 1:1 ratio.

3.3 Study Scheme Diagram

Figure 1 (overleaf) depicts the process of recruitment, intervention and follow up of trial participants.

4 Subject Selection

4.1 Number of Subjects and Subject Selection

People living with ABI that meet the inclusion criteria for the study will be recruited by clinicians in Swansea Bay University Health Board (SBUHB), Hywel Dda University Health Board (HDUHB) and Cardiff and Vale University Health Board (CVUHB) and their support staff. Three research sites were selected as it remains unclear whether this intervention can be replicated beyond SBUHB.

As our trial examines the feasibility of running a full-scale randomised-controlled trial in the future, we intend to calculate the estimated effect size on which the sample size of a future trial could be determined. Based on experience in SBUHB, we feel it is feasible to recruit the required sample of participants (N=60): 10 participants are included per group across three Health Boards.

Local clinical teams at research sites will identify potentially eligible participants and refer them to the Principal Investigator (PI). If deemed initially suitable, the participant will be approached for consent to be formally screened for the trial.

Clear inclusion and exclusion criteria have been developed so that clinicians can appropriately identify and approach potential participants with information regarding the study, and can do so with reasonable confidence that the individual will meet the criteria for inclusion. Importantly, one inclusion criterion is that potential participants must not have significant communication, behavioural or cognitive impairments to such a degree that it would prevent them from engaging in the intervention. This will minimise the risk of distress associated with being unable to engage in the intervention.

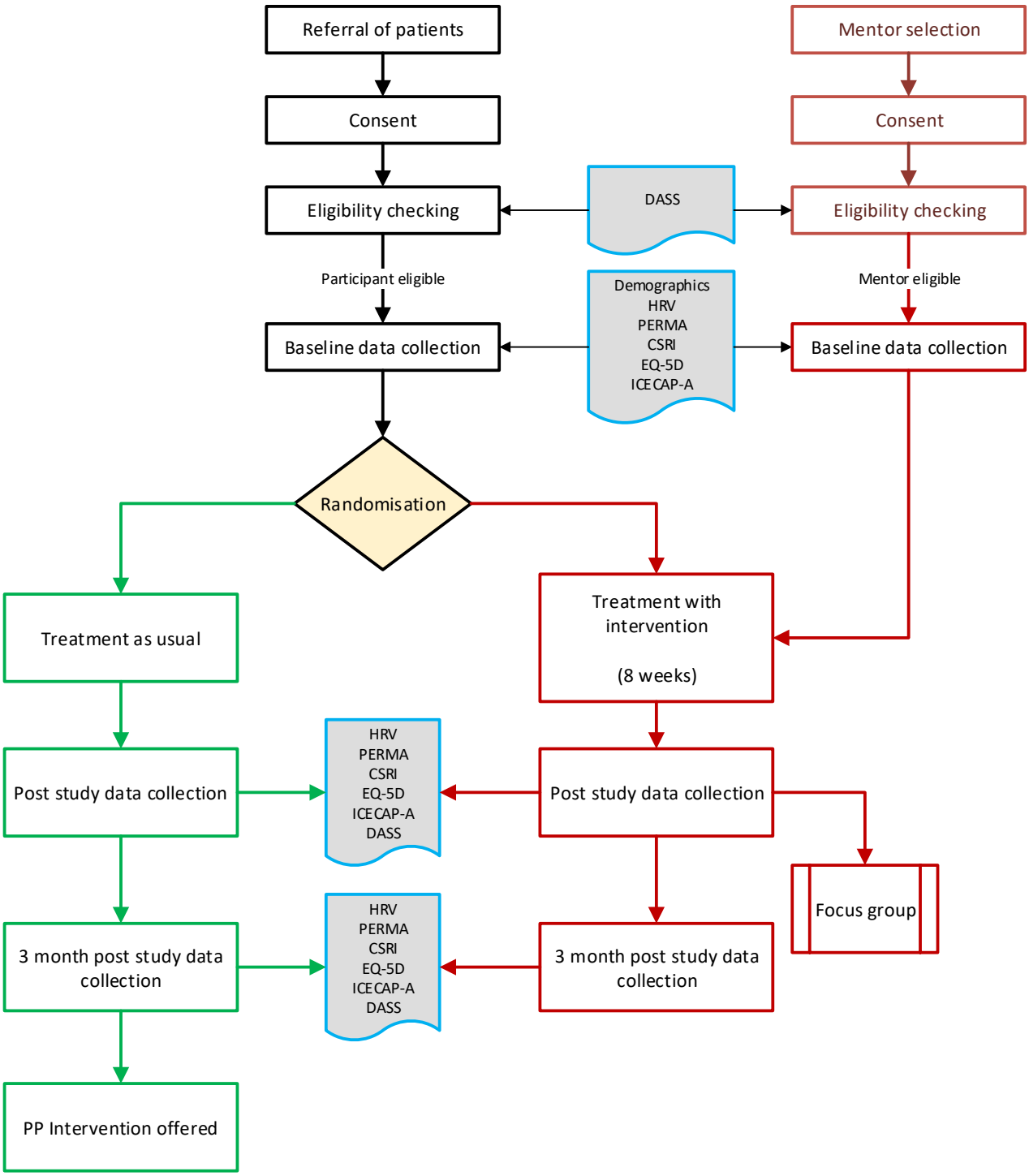

Figure 1: Flowchart of participant and mentor recruitment and follow up.

4.2 Inclusion Criteria – Participants

- Confirmed diagnosis of ABI
- Ability to actively engage in the intervention as determined by their neuropsychological assessment scores and their clinician
- Living in the community
- Psychological distress (evidenced by their scores on the Depression, Anxiety and Stress Scales (Lovibond & Lovibond, 1995): participants with scores greater than 10 for the depression subscale and/or 8 for the anxiety subscale and/or 15 for the stress subscale will be included in the study if they meet the additional study criteria.
- Age eighteen years or older
- Living within the catchment area of one of the participating health boards
- At least three-month post injury at the point of recruitment allowing time for spontaneous recovery and for the person to become aware of their difficulties and the implications of this on their lives

4.3 Exclusion Criteria – Participants

- Receptive or expressive language difficulties, or extremely low memory function that may preclude people from engaging meaningfully
- Medical or psycho-social reasons (based on risk assessment by the referring clinician).
- Potentially disruptive to other group members as determined by their clinician
- Not able to provide informed consent

4.4 Eligibility Criteria – Mentors

Mentors will be subject to the same inclusion criteria as participants with the exception of showing 'evidence of psychological distress.' Mentors will also be subject to the following additional inclusion criteria:

- Known to and recommended by their referring clinical team
- Demonstrated ability to be responsive and sensitive to the needs of others
- Good interpersonal skills
- Willing and able to commit to training as well as attending all 8 treatment sessions

Two mentors will be recruited per group per Health board.

4.5 Criteria for Premature Withdrawal

Participants who are unable to comply with the trial treatment may need to be withdrawn. The PI will decide whether this is an appropriate action and should discuss their concerns with the Chief Investigator (CI) first.

Participants may decide to withdraw themselves from the trial. They need not provide a reason(s) but any information provided will be recorded in the trial database.

5 Study Procedures

5.1 Informed Consent Procedures

Any potential participants and mentors will be asked by a member of their clinical team whether they would like to participate in the study and will be given the participant information sheet (PIS) or Mentor information sheet (MIS). These will explain the trial, what they will be expected to do, and any risks and benefits to being in the trial. Potential participants will be told about the process for withdrawing if they so wish.

Participants who are considering involvement will be provided with the opportunity to talk about the research with a member of the local research team. They can also discuss the research with the research assistant, PI or an appropriate clinician.

The PIS will explain that participants may experience distress associated with talking about their condition. Attempts will be made to minimise any risks associated with distress. This will include the opportunity to discuss with a member of their clinical team. If serious cause for concern is observed, appropriate action may include liaising with a participant's GP. Contact details for the PI and CI will be attached to the PIS. This will enable participants to seek further information or additional clarification if necessary, and will ensure they are fully informed of all aspects of the study. The participant's ability to withdraw at any stage of the study and the process for it will be made clear. In accordance with GDPR guidelines a section will be added to the PIS and MIS outlining what choices the patients have regarding how their research data is used. The PIS and MIS will also clearly explain the limits of confidentiality.

Participants in the control group will not receive the PP intervention during the study period but will be offered the intervention when the study period ends. This will be made clear in the PIS.

No participant will be included in the trial if they do not have the required capacity or decision-making abilities to make an informed decision. Mental capacity assessments are a routine part of the role of clinicians and the clinician who first identifies the participant will ensure that the individual is able to a) understand the information relevant to the decision; b) retain the information over time; c) weigh up the pros and the cons of participation; and d) clearly communicate their decision.

Following the initial provision of study information, participants will be asked to indicate their desire to engage in the study within a week of receiving the PIS/MIS. If they agree to consent, they will agree a convenient date and time to meet with the research assistant (under the supervision of a clinical psychologist) to provide written consent. Ideally, this meeting will be coordinated with one of the patient's routine appointments to minimise any inconvenience to the service user.

Formal eligibility checks will begin at the meeting to determine initial eligibility for the study (see inclusion/exclusion criteria). Consent can only be taken by research team members authorised to do so on the trial delegation log. The consent decision and details about the PIS/MIS (version and date) provided should be documented in the patient's medical records.

A trial ID will be allocated to all consenting participants by the research team. This will be a unique number which will follow the structure below:

> [site ID Swansea = 01; Hywel Dda = 02; Cardiff and Vale = 03] – [Participant = 01 or Mentor = 02] – [Participant number allocated in ascending order] e.g. Swansea Bay UHB = site 01 so their first participant will be 01-01-01, and their first mentor would be 01-02-01.

Participants' capacity to remain in the study will be monitored throughout the different stages of the study by the PI. This ensures that all participants can fully consent to participation and can decide to withdraw at any point. If patients experience distress or upset due to them not having met the eligibility criteria, these individuals will be offered support by their clinical team and the reasons for their change in eligibility will be clearly explained.

5.2 Screening Procedures

Clinical staff will act as referrers for the trial in addition to the PI at the site so that all potential patients can be identified.

The PIs will be asked to assess the medical records of consenting participants and provide information regarding the diagnosis of the ABI and the severity of the injury according to relevant clinical markers presented within the medical records. For instance, a diagnosis of 'traumatic' brain injury would follow in lieu of information relating to the duration of post-traumatic amnesia, in addition to the Glasgow Coma Score following the incident and the duration of loss of consciousness. This information allows clinicians to classify injuries as mild, moderate or severe and offers greater insight into the prognosis and potential mediators of treatment effects. This information will be included in the referral letter to the community service and will be passed on with the consent of the patient.

Neuroimaging data will also be sought from the medical records to aid the clinician in understanding the effect of a patient's ABI. The PIS states clearly that this information will be accessed by the PI from the medical records.

Consenting participants and mentors will be screened by an authorised person (on the trial delegation log) to ensure that they are suitable to be involved in the trial. This will involve:

1. Cross referencing against the eligibility criteria
2. Completion of the Depression, Anxiety and Stress Scale (DASS) questionnaire
3. A brief cognitive assessment

Any participants deemed ineligible will be followed up by their clinician.

5.3 Randomisation Procedures

Participants will be randomly allocated to the intervention (8 PP meetings) or treatment as usual (TAU).

Randomisation will be done using the trial database (REDCap) by an authorised person once eligibility has been confirmed. The participant will be notified of the allocation and for those allocated the intervention, meeting dates will be provided.

Randomisation will be stratified to ensure that the intervention and control group sizes and the number of patients with anti-depressant use are equivalent between groups.

5.4 Schedule of Treatment for each visit

Participants (P) and mentors (M) will attend the following trial visits:

Activity	Time point				
	Eligibility Checks	Baseline Assessments	Meetings (1-8)*	Once meetings completed	3m later
Consent	P, M				
Eligibility checks	P, M				
• RBANS	P, M				
• SASNOS	P, M				
• DASS-21*	P, M			P,M	P,M
Data collection					
• HRV		P, M		P, M	P,M
• PERMA Profiler		P, M		P, M	P,M
• EQ-5D-5L		P, M		P, M	P, M
• ICECAP-A		P, M		P, M	P, M
• Demographics		P, M			P, M
• CSRI		P, M			P,M
Randomisation		P			
Attend meetings			P**, M		
Focus group					P**, M

**DASS used for eligibility and used as baseline data (not repeated in baseline session)*
*** Intervention group only. TAU participants do not attend meetings or the focus group*

5.5 Summary of the content of the 8 week intervention

A **treatment manual** will be developed for sites to provide a standardised intervention. The list below summarises the topics to be covered at each session.

Session One – Managing Negative Emotions and Introduction to Positive Psychology: Before focusing on positive emotions and wellbeing, we argue that it is important to acknowledge the role of negative emotions.

Following a major life event like a brain injury, the experience of negative emotion is both understandable and common. It is important to recognise this and point out that the aim of this course is not to 'get rid' of negative emotions as this is not possible. Instead, we can learn skills to deal with the negative life stressors as well as possible.

Session Two - Character strengths: Identifying one's character strengths is the foundation to 'building on what is strong, rather than fixing what is wrong'. Ryan Niemiec's work provides a solid foundation in this regard.

Session Three – Body Mind Connections and Positive Health Behaviours: Recent research highlights that positive psychological interventions may be associated with smaller effect sizes than prior studies suggested. We emphasise here the importance of building positive health behaviours to facilitate vagal function that will have positive impacts on psychological experience, based on our GENIAL model. We further draw upon behaviour change theory to reinforce and sustain positive behavioural change.

Session Four – Positive Emotions and Flow: Positive emotions are fundamental to theories of hedonic wellbeing. Barbara Fredrickson's 'Broaden and Build Model' is a major focus of this section. A core feature of positive psychology is to promote task engagement by facilitating 'psychological flow' as coined by Mihály Csíkszentmihályi. Flow is facilitated through activities that involve both a high level of skill and challenge.

Session Five – Meaning, Purpose and Achievement: Meaning and purpose in life are major component to eudaimonic wellbeing. The work by Viktor Frankl and Paul Wong are particularly influential in this regard. We argue that meaning and purpose in life might be enhanced and facilitated through a combination of interventions that focus on the individual, community and environment. Achievement orientation is also considered to be a fundamental component to the promotion of wellbeing. Influencers include Angela Duckworth and Carol Dweck.

Session Six – Connecting with Nature and Positive Emotions: A more moral and ethical science of wellbeing is needed that tackles criticisms of positive psychology relating to western neoliberalism and rampant individualism. We emphasise a need for reconnecting with nature and in doing so, suggest that a modern science of wellbeing could be applied to tackle major societal challenges including the climate crisis. Víctor Corral Verdugo's work specifically links positive psychology to sustainability.

Session Seven – Social Relationships: Our original GENIAL model emphasised the need to move beyond a focus on the individual given recent findings highlighting the impacts of social ties on health and wellbeing. We emphasise here the need to focus on positive social relationships to facilitate individual wellbeing in line with Alex Haslam's 'social identity theory'.

Session Eight – Optimism, Hope and Post Traumatic Growth: Hope and optimism have a lot in common. Both involve having a positive outlook on the future. It is often the case people with stroke or brain injury report feeling far less hopeful and optimistic than the general population In this session, we emphasise the possibility of a positive trajectory through brain injury recovery.

Patients with ABI can experience difficulties with emotional regulation and they may find it more difficult to control negative emotions and have an increased tendency to experience irritability and anger. Physical difficulties after brain injury can interact with the environment. For example, long complex sessions can increase fatigue/overload leading to frustration. Noise may cause overload because participants affected by brain injury may find it difficult to filter out irrelevant stimuli leading to frustration, mistakes, distractibility, fatigue and headaches. All of the interventions will be staffed by clinicians who are experienced in managing such behaviours and running therapeutic groups. Clinicians will establish shared group 'ground rules' at the beginning of the intervention to promote a safe, calm and respectful environment.

5.6 Follow up Procedures (if applicable)

Participants in the intervention group will be invited to attend a focus group once the PP meetings have ended. They will be asked about their opinions on the meetings, the intervention and how they felt about being in the trial.

Participants in the control group will not attend the focus groups because they will not have had the intervention.

Three months after the PP group meetings have ended, the final data collection will be done. For the TAU group, the 3m data will be collected during the same time period as the 3m follow up data is collected from participants in the intervention group (three months after the PP meetings end).

5.7 End of Study Definition

The study will end once the last focus group has been completed and has been transcribed and all data has been collected at the 3m follow up period.

5.8 Procedures for unblinding

No blinding is required for this trial.

5.9 Subject Withdrawal

Participants and mentors may withdraw from the trial at any time without giving a reason(s). Any reasons provided should be recorded by the research team and reviewed as part of the primary outcome analysis.

5.10 Data Collection and Follow up for Withdrawn Subjects

Participants who withdraw will have their data included in the trial unless they explicitly ask for their data to be removed. Where identification allows, this will be done.

6 Safety Reporting

6.1 General Definitions

Adverse Event (AE)
An AE is any untoward medical or clinical occurrence in a subject to whom an intervention has been administered, including occurrences which are not necessarily caused by or related to the intervention. An AE can therefore be any unfavourable and unintended sign, symptom or disease temporarily associated with trial activities. We expect some psychological distress to be present in the form of anger, anxiety or/and depression as these are common experiences after a brain injury and the presence of these difficulties are part of the eligibility for the trial. Accordingly, it is not necessary to report all events involving participants anxiety, depression, anger and stress unless they increase in severity during the trial. The PI at the sites are responsible for making a clinical decision regarding the significance of the distress.
As a function of the brain injury it will also be common for participants to experience dizziness, cognitive difficulties, headaches and fatigue. These will only be reported if they increase in severity throughout the trial as assessed by the PI for each site.

Serious Adverse Event (SAE)
An SAE fulfils at least one of the following criteria:

- Is fatal
- Is life-threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent, significant or further disability/incapacity

- Is a congenital anomaly/birth defect
- Is otherwise considered medically or clinically significant by the Investigator

6.2 Investigators Assessment

Seriousness - The PI or delegate responsible for the care of the patient, is responsible for assessing whether the AE is serious according to the definitions given in section 6.1.

Causality - The PI must assess the causality of all SAEs in relation to the trial treatment according to the definition given. The (S)AE may be unrelated, possibly related, probably related or definitely related to the intervention received.

Expectedness - The PI or delegate must assess the expectedness of all SAEs according to the definition given. If the SAE is unexpected and related, then it needs immediate reporting.

Severity - The PI must assess the severity of the event according to the following terms and assessments. The intensity of an event should not be confused with the term "serious" which is a regulatory definition based on patient/event outcome criteria:

Mild: Some discomfort noted but without disruption of daily life
Moderate: Discomfort enough to affect/reduce normal activity
Severe: Complete inability to perform daily activities and lead a normal life

6.3 Notification and reporting Adverse Events or Reactions

If the AE is not defined as serious, the AE is recorded in the trial database and the participant is followed up by the research team. The AE must also be documented in the participants' medical notes (where appropriate) and the CRF.

Preventative measures have been put in place in the development of the intervention. For example, group content and materials have been co-designed alongside service users based on their experiences. The sessions include breaks and a balance between listening and interacting. No participants will be included in the study if they are considered too great a risk by the clinical team (i.e. significant forensic history, uncontrolled epilepsy etc.) or it is felt that they will be disruptive in a group setting.

The local research team will record any AEs reported by participants either during a meeting or in between meetings on the appropriate paperwork and they should be assessed by an authorised person (on the delegation log) as per section 6.2. All AEs should be reported within 24 hours of becoming aware of the event. All AEs will be followed up by the clinician in the research team at the site.

Responding to questionnaires or interview questions may potentially be upsetting to participants. Prior notice of this possibility will be documented in the PIS. Participants will have the opportunity to discuss any concerns they have during or after completing the battery of questionnaires, or the interviews. They will be informed from the start of their right to stop at any time during this process. Attending group sessions may include topics that individuals find upsetting (e.g. the impact of ABI on their wellbeing). Any adverse reactions may be addressed during the sessions if appropriate or in confidence outside sessions (by the PI for the study). In a crisis situation, the PI will notify the patients GP in accordance with clinical governance procedures. The limits of confidentiality will be made explicitly clear on the PIS.

6.4 Notification and Reporting of Serious Adverse Events or Reactions

Serious Adverse Event (SAEs) will be notified to the Trial Office by the site PI or other authorised person. The Trial Office (on behalf of the CI) will:

-Report to Sponsor within 24 hours of learning of the event
-Report to the REC within 15 days of learning of the event

Serious Adverse Event (SAEs) that are considered to be 'related' and 'unexpected' (i.e. a SUSAR) are to be reported to the sponsor within the same timeframes.

6.5 Urgent Safety Measures

The CI may take urgent safety measures to ensure the safety and protection of the clinical trial subjects from any immediate hazard to their health and safety, in accordance with Regulation 30. The measures should be taken immediately. It is the responsibility of the CI to inform the sponsor and REC (via telephone) of this event **immediately**.

The CI has an obligation to inform the REC **in writing within 3 days**, in the form of a substantial amendment. The sponsor must be sent a copy of the correspondence with regards to this matter.

Should relevant information surface during the research project, the trial co-ordinator will discuss the information with the CI and PIs and co-ordinate a plan to ensure participants are made aware of this information. For example, whether or not the researcher should contact a participant directly, or if it would be more appropriate for a member of their care team to contact them, will be discussed and will depend on the nature of the information in question.

6.6 Annual Safety Reporting

The CI will send the Annual Progress Report to the REC using the NRES template (the anniversary date is the date on the REC "favourable opinion" letter from the REC – January 2020) and to the sponsor.

7 Statistical Considerations

As the primary focus of this trial is to determine the feasibility of the design, our primary endpoints are based around measuring the criteria stated in Section 3.1 as follows:

Criteria	Measurement
Recruitment: Can we recruit and retain enough participants? Are retention rates comparable with previous rates reported for psychotherapeutic groups? Can we determine effect size to inform sample size calculation needed for a larger trial? Can we identify reliable recruitment pathways across the sites? What are the characteristics of the referred sample and who is eligible? In practice what are the reasons for deeming someone ineligible and how do participants experience the process to manage this? Is the patient facing information fit for purpose? Do we need to refine this information based on patient feedback?	Number of participants recruited. Number of participants declining and reasons for declining Number of participants retained.
Interventions: Will clinicians and mentors comply with formal training needed to run the intervention in a standardised way? Is the intervention acceptable to participants? How many sessions did they attend? Is the treatment manual acceptable? What was the homework compliance rate and how do this compare to similar studies	Number of treatment sessions completed (must be at least 6 to be successful). Proportion of homework completed Adherence to the treatment manual as assessed review of randomly selected recordings of the intervention delivered at three sites.
Randomisation Process and Blinding: Can assessors predict whether the participant was in the TAU or PP group?	Success would be indicated if assessor's predictions of group allocation (TAU or PP) were at chance levels, as per Cullen et al. 2016
Data collection, quality, management and analysis: Do participants find the evaluation measures and HRV monitoring acceptable, what are completion rates and loss to follow-up rate and are these comparable to previous work (e.g. Cullen, 2018- 55% of eligible participants were enrolled on the study and 63% of participants were retained to the 20-week follow-up	Success would be indicated if completion rates for post-intervention assessment and follow up data collection were comparable to previous work (e.g. Cullen, 2016).

assessment). Is the data analysis plan to deal with missing data and trial database fit for purpose?	
Research Governance and trial management: Are the local risk management plans, adverse events procedures and health and safety procedures fit for purpose and are the research team and clinicians involved in recruitment and delivery of the intervention compliant?	Success would be indicated by compliance with local and national policies underpinning research governance (e.g. completion of site-specific risk assessments, management plans and documentation of adverse risks). Success will also be determined if the study is completed on time.

7.1 Safety Endpoints

We will assess AEs as they are reported and will determine whether they are relevant to the trial design and the intervention at regular intervals. The data will be reported to the Trial Steering Committee at regular intervals.

7.2 Sample Size

We aim to recruit up to 60 eligible participants, considering up to 50% of participants will drop out of the study.

As this is only a feasibility trial, we consider this number sufficient to test the design we propose and to assess the trial against the ACCEPT criteria to determine whether a full-scale trial can be done.

7.3 Statistical Analysis

Primary outcomes will be determined by the ACCEPT checklist (Charlesworth et al., 2013) and evaluated by the Trial Management Group in consultation with the Trial Steering Committee. Using this checklist, the researchers will determine whether:

a) it is possible to recruit sufficient numbers of participants;
b) study procedures and the intervention are suitable and acceptable;
c) data collection procedures are feasible;
d) the research team has the resources to manage a full-scale RCT.

7.3.1 Quantitative data analysis

Analysis will focus on descriptive statistics and feasibility outcomes. While clinical effectiveness will not be formally evaluated at this stage, we will inspect quantitative data for early evidence that the intervention shows promise or, conversely, appears unlikely to result in the desired outcome.

It is hypothesised that measures of DASS will diminish, and measures of PERMA and HRV will improve consistent with expected in improvements in wellbeing using a mixed effects analysis of variance with group as a between-subjects factor and time as a within-subjects factor. We will estimate the treatment effect size and intra-group dependencies which will be used to calculate the sample size

7.3.2 Health economic analysis

We will test the feasibility of collecting the data required for a full economic evaluation (cost-utility and cost-effectiveness analyses are planned to be conducted as part of a future trial). We will provide a provisional estimation of the resource use and costs of the PP intervention compared to TAU from an NHS and Personal Social Services (PSS) perspective. We will establish the costs of the intervention and describe the healthcare resource use and associated costs over the course of the follow up of the trial for the PP intervention compared to TAU. We will produce a simple cost consequence analysis to present a provisional estimation of the costs and outcomes of the PP intervention and TAU and to inform the selection of the costs and outcomes that will be most relevant in a future definitive trial.

7.3.3 Qualitative data analysis

A Qualitative Data Analysis Plan (QDAP) will be developed according to Swansea Trials Unit (STU) SOPs to specify the procedures to be followed when analysing and reporting the qualitative data. The QDAP will document how the data will be managed, analysed and reported. Thematic analysis will be used to explore key themes/codes that

emerge from the data. The data will be analysed whilst the study is commencing and a codebook will be developed following the first series of transcriptions to provide a formalized operationalization of the codes/themes identified (Fereday and Muir-Cochrane 2006; Fonteyn & Bauer-Wu, 2008). The code book will be locked before the last focus group. The remaining data will then be coded using the codebook and key themes relating to feasibility will be outlined and reported.

8 Data Handling & Record Keeping

8.1 Confidentiality

The local PI (also members of the clinical teams) will access patient records in order to identify potential participants and to get information regarding the diagnosis and severity of injury. No other member of the research team will need to access clinical notes.

In order to minimise risks associated with breaches of data protection, personal identifiable information will be stored securely in a locked cabinet or in password-protected electronic files on NHS premises.

To minimise confidentiality breaches, only one database will include patient identifiable information and this will be stored on the Swansea Bay NHS secure server, and not on one specific laptop device. This database will link the patient to their unique reference number and provide a means to cross-reference this with the patients name, age, and information about their brain injury. All outcome measures completed by research participants throughout the course of the study (including questionnaire and heart rate data) will state the unique reference number assigned to the participant and will not include the individual's name.

Consent forms will be stored in the patient's clinical notes, in addition to the letter informing their GP of their involvement in the study. Only fully anonymised data will be sent via email to Swansea University for analysis.

Personal laptop computers and university laptops may be used to analyse and write up fully anonymous data. NHS iPads will be used to record audio data from the focus groups. The NHS iPads are appropriately networked, such that the audio files can be uploaded directly to NHS servers rather than the iPad itself. The audio files will be stored on the secure NHS network. The audio data will be transcribed by a member of the research team. With respect to quotes obtained during the focus groups, no quote will be published that identifies the participant or other participants in the group.

Heart Rate Variability (HRV) Monitors data will be used to measure heart rate variability. HRV data is recorded on the monitors themselves that can then be downloaded to an NHS laptop. We are using a monitor called First Beat Body Guard 2. Following data collection, the data will be uploaded immediately from the device using an 'offline mode' to a secure NHS network. The uploaded data contains information about heart rate variability but no personal data that can identify a participant. The data collected will be deleted as soon as it is taken off the device.

The database linking data to personal identifiable information will be password protected and stored on the secure NHS network at SBUHB - not on any device itself. This identifiable information is only accessible by the research assistant and PhD student. This is necessary because they will need to know the person's name and research number in order to give out questionnaires and collect HRV data.

Data will be kept in a locked filing cabinet at the brain injury department associated with each research site. This data will be retained for five years in line with health board guidelines, before being destroyed. Audio-recordings and transcription data relating to the qualitative research component will be stored on password-protected documents on a secure NHS network at SBUHB. No personal patient information will be stored on iPads or laptop devices. The database which links each participant and details of their medical information to their unique research number will be stored on a secure NHS network and password protected. It will never be stored on any device and paper copies are not required.

Upon entering the study, participants will be assigned a Trial ID. This code helps to maintain participants anonymity throughout the research study. This unique code and the outcome data relating to the study will be stored on an excel

spreadsheet separate from the main personal identifiable data (which will be stored separately on secure NHS network). Adherence to the NHS code of conduct will be followed.

Participants assigned to the PP group will be invited to focus groups after the intervention. The focus groups will be audio-recorded. Participants will be asked not to disclose any personal information about themselves or other participants during the focus group. The importance of this will also be stated on the PIS and the MIS for mentors. Should a participant accidentally disclose any personal information which could identify them or another group member the audio file will be stored on an NHS networked computer and transcribed as quickly as possible. Any information that could identify individuals in the group will be omitted from the transcription and the audio file will then be deleted. The audio data will be transcribed by a member of the research team.

The trial coordinators (employed by SBUHB), and a research assistant (PhD student) and the PI's at their own research site will have access to personal data collected in the study. This is clearly outlined in the PIS, MIS and corresponding consent forms. The trial coordinators and PhD student will have research passports at all three sites and collect data across the three research sites (CVUHB, HDUHB and SBUHB). The trial coordinators and PhD student will need access to personal data as they will be collecting the data at each site and anonymising it at each site. The trial coordinators will give paper-based indefinable data to the PI to store in a locked filing cabinet. Paper-based questionnaire data containing only the Trial ID will be taken and stored at the brain injury service in SBUHB for analysis, as this is where the trial coordinators will be based. There will be one database that links participant's names with their research identification number and this information will be password-protected and stored on a secure NHS network in SBUHB. Only the trial coordinators, PhD assistant and the PIs at each site (clinicians in the brain injury team) will have access to this database.

No personal data that will connect an individual to the study will be published. Demographic data collected will only be reported to describe the composition of the groups. Individuals will not be described nor any information that could identify individuals in the group. All other information and data collected will be fully anonymous. Participants will be informed on the PIS/MIS that direct quotes from focus groups may be used in the write up but that they cannot be identified from this information

8.2 Study Documents

As well as a signed protocol and any subsequent amendments to the protocol, we will also have the following associated documents for the trial:

- Treatment manual
- Sponsor Self-Monitoring template for the trial team to complete on a regular basis as detailed by the Monitoring section
- Current/Superseded Patient Information Sheets (as applicable)
- Current/Superseded Consent Forms (as applicable)
- Indemnity documentation from sponsor
- Conditions of Sponsorship from sponsor
- Conditional/Final R&D Approval
- Signed site agreements
- Ethics submissions/approvals/correspondence
- CVs of CI and site staff
- Delegation log
- Staff training log
- Enrolment log
- Correspondence relating to the trial

8.3 Case Report Forms and questionnaires

We will use paper Case Report Forms (CRFs) to collect clinical data at baseline for eligibility, safety and withdrawal data where it is not feasible to enter directly onto the REDCap database. The database will hold all meeting dates and attendance information.

Participants will complete paper questionnaire booklets which will contain the following questionnaires:

- Depression, Anxiety and Stress Scales (DASS)
- St Andrews-Swansea neurobehavioral outcome scale (SASNOS)
- Repeatable battery for assessment of neuropsychological status (RBANS)
- EQ-5D-5L
- ICECAP-A
- Perma profiler
- Client Service Receipt Inventory (CSRI) – Mental Health

Where possible, the participant will verbally convey their response and a researcher will type the response directly into the database.

The participant's heart rate variability will also be recorded electronically, using a heart rate monitor. This will be carried out to provide maximum privacy for the participant.

8.4 Qualitative data

Semi-structured questionnaires will be used in focus groups to facilitate a better understanding of the impact the intervention has had, identify components participants like and dislike, and solicit feedback from people living with ABI in relation to what does and does not work. A theory-driven topic guide has been developed to form the basis of semi-structured interviews for use in the qualitative focus groups, with reference to the consolidated criteria for reporting qualitative research (COREQ). The topic guide for focus groups will be flexible and may be revised throughout the data collection process, consistent with established guidelines (Charmaz, 2014).

8.5 Record Retention and Archiving

Quantitative data will be managed using a REDCap system hosted at Swansea University. REDCap a web-based system providing a straight-forward user-interface with validated data entry, audit trails and central data query monitoring, and processes to export data to common statistical packages.

Research data linking a person's name with their Trial ID will be kept on an NHS secure network at SBUHB. It will remain on the network and deleted 5 years after the study has ended.

All patient-identifiable information stored in the NHS (with the exception of entries in clinical notes) will be destroyed within 5 years of the start of the study. Fully anonymised data stored at Swansea University will be destroyed after 10 years, in adherence to university policy.

8.6 Compliance

The CI will ensure that the trial is conducted in compliance with the principles of the Declaration of Helsinki (1996), and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework, Trust and Research Office policies and procedures and any subsequent amendments.

8.7 Clinical Governance Issues

This protocol and any subsequent amendments, along with any accompanying material provided to the participants and mentors in addition to any advertising material will be submitted by the CI to the corresponding REC. Written Approval from the REC must be obtained and subsequently submitted to the Research & Development Departments to obtain Final R&D approval.

8.8 Quality Control and Quality Assurance

The research sponsor (Swansea Bay University Health Board Research and Development Department) will ensure arrangements and systems are in place for the management and monitoring of research, in accordance with Good Clinical Practice guidelines.

All aspects of the feasibility trial will be evaluated using the standardised ACCEPT checklist (Charlesworth et al. 2013).

The research team will be responsible for monitoring and auditing the conduct of the study in accordance with the Research Governance Framework. Several members of our research team work in STU who have the expertise to guide and oversee the trial.
The TSC will oversee the work of the research team and will comprise a chairperson, an expert in the field, an independent statistician and at least two additional public patient representatives.

8.8.1 Summary Monitoring Plan

Although a risk-based assessment will often build in flexibility for monitoring activities, ICH E6 R2 requires sponsors to periodically review their risk control measures to ascertain whether the quality management activities that have been implemented remain effective and relevant. The results of monitoring may direct changes to the monitoring assessment/strategy; either moderation (downgrading of activities) or escalation of activities. The Quality Assurance Officer can alter the visit timeframes depending on the monitoring findings.

A Quality Assurance programme is in place to ensure adherence to the protocol. Major and minor deviations will be collected. Each visit will verify that the rights and wellbeing of participants are protected. Accuracy, completion and validity of reported trial data from the source documents, evaluation of the conduct of the trial with regards to GCP, compliance with the currently approved protocol, and within the applicable regulatory requirements will also be verified.

8.8.2 Audit and Inspection

Auditing: Definition "A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s)."

A study may be identified for audit by any method listed below:
1. A project may be identified via the risk assessment process.
2. An individual investigator or department may request an audit.
3. A project may be identified via an allegation of research misconduct or fraud or a suspected breach of regulations.
4. Projects may be selected at random. The Department of Health states that Health Boards should be auditing a minimum of 10% of all research projects.
5. Projects may be randomly selected for audit by an external organisation.6. Internal audits will be conducted by a sponsor's representative.

8.9 Non-Compliance

Definition of non-compliance: A noted systematic lack of both the CI and the study staff adhering to SOPs/protocol/ICH-GCP, which leads to prolonged collection of deviations, breaches or suspected fraud.

Non-compliance may be captured from a variety of different sources including monitoring visits, CRFs, communications and updates. The sponsor will maintain a log of instances of non-compliance to ascertain if there are any trends developing which need to be escalated. The sponsor will assess non-compliance and determine a timeframe within which they need to be dealt with. Each action will be given a different timeframe dependent on the severity. If the actions are not dealt with accordingly, the R&D Office will agree an appropriate action, including an on-site audit.

9 Trial Committees

The trial team (Chief Investigator, Principal Investigator for Swansea Bay, trial coordinators, trial manager and other contributors as required) will meet on a fortnightly basis during set up and early stages of recruitment which may be extended to monthly at a later point.

A Trial Management Group (TMG) will convene on a quarterly basis to discuss trial progress. This group will comprise of the trial team, PIs from other sites, an expert in the field, a sponsor representative and at least one patient or public representative. Ad hoc meetings may be called if the need arises.

A Trial Steering Committee (TSC) will be convened to independently oversee the trial and will also act as the Data Monitoring Committee. The committee will consist of a Chairperson who is an expert in the field, at least one other clinical person, an independent statistician and at least one patient or public representative. All independent members will agree to a Charter prior to commencing their role.

10 Publication Policy

The main findings of the study will be made available via written feedback. Aggregate data and findings will also be submitted for publication in scientific journals and presentation at academic conferences. All data presented in dissemination will be fully anonymised. Participants will be informed that direct quotes may be taking from focus groups and used in the final write up.

We will present our findings at local, national, and international conferences, welcoming attendance by service users and providing opportunities for service users to be informed and involved in disseminating the work through the co-facilitation of presentations, workshops and publications. We will liaise with Health Board and University communications departments, as well as charities to identify further dissemination opportunities via social media, newsletters, magazines and websites. We will also seek out opportunities to present the work to local stakeholders and seek their advice to identify effective ways to disseminate what we learnt to people living with ABI.

Participants have the option of receiving written feedback detailing a summary of the research. They can indicate their preference to receive a summary of the results on the participant consent form.

Participants will be provided with the researcher's contact details should they wish to discuss anything further. If appropriate, findings may also be communicated on the local NHS health board's website and if so, participants will be informed of how to access this information at the web address.

Authorship on resulting publications will be determined on the basis of standard guidelines for authorship such as those from the International Committee of Medical Journal Editors.

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12 Appendices

12.1 Appendix 1 – Information with regards to Safety Reporting in Non-CTIMP Research

	Who	When	How	To Whom
SAE	Chief Investigator / Clinical Lead	-Report to Sponsor within 24 hours of learning of the event -Report to the MREC within 15 days of learning of the event	SAE Report form for Non-CTIMPs, available from NRES website.	Sponsor and MREC
Urgent Safety Measures	Chief Investigator / Clinical Lead	Contact the Sponsor and MREC Immediately Within 3 days	By phone Substantial amendment form giving notice in writing setting out the reasons for the urgent safety measures and the plan for future action.	Main REC and Sponsor Main REC with a copy also sent to the sponsor. The MREC will acknowledge this within 30 days of receipt.
Progress Reports	Chief Investigator	Annually (starting 12 months after the date of favourable opinion)	Annual Progress Report Form (non-CTIMPs) available from the NRES website	Main REC
Declaration of the conclusion or early termination of the study	Chief Investigator	Within 90 days (conclusion) Within 15 days (early termination) *The end of study should be defined in the protocol*	End of Study Declaration form available from the NRES website	Main REC with a copy to be sent to the sponsor
Summary of	Chief	Within one year of	No Standard Format	Main REC with a

final Report	Investigator	conclusion of the Research	However, the following Information should be included:- Where the study has met its objectives, the main findings and arrangements for publication or dissemination including feedback to participants	copy to be sent to the sponsor