

Actissist 2.0: Active Assistance for Psychological Therapy 2.0 (Actissist 2.0): Digital Intervention for Co-producing care in psychosis

Statistical Analysis Plan (SAP)

**Version:** 1.0

**Authors:** Gordon Forbes, Richard Emsley

**Date:** 05/06/2020

**Protocol version:** This SAP has been written based on Protocol V10

**Trial registration:** ISRCTN76986679, registration date: 05/02/2018

**Version history:**

| Version: | Date:      | Changes:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----------|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 0.1      | 20/04/2020 | First draft of SAP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 0.2      | 21/04/2020 | Additional analysis code added                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| 0.3      | 24/04/2020 | Additional details on outcomes scoring added.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 0.4      | 05/05/2020 | Additional details on outcomes scoring added. Description of analysis of health economic data added.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 0.5      | 22/06/2020 | Analysis of outcomes relating to cannabis use restricted to cannabis users at baseline.<br>Partially missing data in primary outcome due to telephone completion (items n1, g4, g5) to be prorated.<br>Inferential analysis of TLFB to be carried out at both 1 month and three months (previously was 3 months only).<br>A criteria for conducting a sensitivity analysis looking at the impact of COVID-19 on outcomes has been added.<br>Subgroup analysis comparing treatment effect for different versions of the app has been added.<br>Reverse scoring of some items of IMSI added to derivation of outcomes<br>Reverse scoring of some items of ERS added to derivation of outcomes. |
| 1.0      | 29/06/20   | Signed version circulated                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |


**Chief Investigator: Professor Sandra Bucci**

Signature  Date 29 June 2020


**Trial Statistician: Professor Richard Emsley**

Signature  Date 2 July 2020

**Trial Steering Group Chair: Professor Max Birchwood**

Signature  Date 16th July 2020

**Trial Steering Group statistician: Bonnie Cundill**

Signature  Date 31st July 2020

## Contents

|                                                       |    |
|-------------------------------------------------------|----|
| Contents .....                                        | 3  |
| Quantitative Analysis Plan .....                      | 4  |
| 1. Brief description of the trial .....               | 5  |
| Trial design.....                                     | 5  |
| Sample size .....                                     | 5  |
| Randomisation procedure, allocation concealment ..... | 5  |
| Blinding .....                                        | 5  |
| Eligibility screening .....                           | 6  |
| 2. Outcome measures .....                             | 7  |
| Primary outcome .....                                 | 7  |
| Secondary outcomes .....                              | 7  |
| App Engagement .....                                  | 8  |
| Health economic outcomes.....                         | 8  |
| 3. General analysis principles .....                  | 8  |
| 4. Data summary and reporting .....                   | 9  |
| 5. Statistical methods for inferential analysis ..... | 10 |
| Analysis of primary and secondary outcomes.....       | 10 |
| Analysis of app engagement .....                      | 10 |
| Analysis of health economic outcomes.....             | 10 |
| Missing data.....                                     | 11 |
| Imputation and pro-rating.....                        | 11 |
| Assumptions for primary analysis .....                | 11 |
| COVID-19 pandemic .....                               | 11 |
| Accounting for versions of Actissist.....             | 12 |
| 6. References .....                                   | 13 |
| Appendix 1 Example analysis code.....                 | 14 |
| Variable names .....                                  | 14 |
| Analysis code .....                                   | 14 |
| Appendix 2: Deriving outcomes .....                   | 15 |
| Scoring rules for outcomes.....                       | 15 |
| Appendix 3: CONSORT diagram.....                      | 17 |
| Appendix 4: Draft tables.....                         | 18 |

## **Quantitative Analysis Plan**

This document details the presentation and analysis strategy for the primary papers reporting results from the Actissist 2.0 trial. It is intended that the results reported in these papers will follow the strategy set out herein; subsequent papers of a more exploratory nature will not be bound by this analysis plan but will be expected to follow the broad principles laid down for the primary paper(s). The principles are not intended to curtail exploratory analysis or to prohibit sensible statistical and reporting practices but they are intended to establish the strategy that will be followed as closely as possible in analysing and reporting the trial.

Health economic outcomes are addressed briefly however this plan does not include a health economic analysis.

## **1. Brief description of the trial**

### **Trial design**

Actissist is a parallel-group randomised controlled trial, with 1:1 allocation and blinded assessors, to test the efficacy of the Actissist intervention in reducing severity of symptoms in people with psychosis when added to Treatment as usual (TAU), compared with routine symptom monitoring plus TAU.

### **Sample size**

The planned sample size was 170 participants recruited over 19 months. 63 per group will give 80% power to detect an effect size of 0.4 (6 points on the PANSS with an SD of 15), based on a two-group t-test with a 0.05 two-sided significance level, assuming a baseline-endpoint correlation of 0.6. Allowing 20% loss to follow-up, in order to maintain 80% power, we will recruit 85 patients per group (N=170). The SD, correlation and attrition rate are based on figures from Actissist 1.0.

### **Randomisation procedure, allocation concealment**

The randomisation process is conducted by a remote internet-based randomisation service ([www.sealedenvelope.com](http://www.sealedenvelope.com)). The allocation sequence will be developed using a computer random number generator to allocate participants on a 1:1 ratio, stratified by service (early intervention vs community mental health).

The randomisation list will be kept by the remote randomisation service ([www.sealedenvelope.com](http://www.sealedenvelope.com)) and kept separate to the collection of outcomes on the study database. The randomisation list will only be revealed to the researchers once all the recruitment is completed.

### **Blinding**

The assessment of the primary outcome will be blinded. Blindness of raters is ensured using a variety of procedures, including briefing participants prior to assessment not to disclose their allocation and data protection of randomisation information. RAs will remain blind to group allocation. An RA who did not conduct the phone set up session will conduct the follow up assessment to maintain the blind. The project officer, or a member of the research team independent to the follow up procedure, will book follow up appointments to further ensure blinding is maintained. Unblindings will be regularly monitored and recorded. Deliberate unblinding would only occur in the case of a serious adverse incident such as risk towards self/others by a participant. The trial statisticians will be partially blinded during the analysis by withholding the identity of the randomised groups and only once the analysis is completed and interpreted will these be revealed. Due to the nature of the intervention, all participants will be unblinded and fully aware of their allocation to the intervention or control groups.

**Eligibility screening**

*Inclusion criteria:*

i). Either:

1) Meet ICD-10 criteria for a schizophrenia-spectrum diagnosis (ICD codes F20, F22, F23, F25, F28, F29) as confirmed by the treating clinician;

OR

2) Meet the early Intervention for Psychosis Service entry criteria, operationally defined using the Positive and Negative Syndrome Scale (PANSS) and/or the psychosis transition criteria of the Comprehensive Assessment of At-Risk Mental States (CAARMS);

ii) in contact with mental health services;

iii) within 5 years from onset of first psychotic episode, deemed by the treating clinician;

iv) meet a criterion level of positive symptoms severity, indicated by a score of >3 (symptom present) on any PANSS positive item and a score of >3 (symptom present) on any PANSS negative or PANSS general items;

v) English speaking;

vi) aged 16 years or older;

vii) capacity and willingness to provide informed consent;

viii) not currently participating in another trial.

*Exclusion criteria:*

i) Anyone with psychosis not in contact with a NHS mental health service.

ii. Anyone less than 16 years old at the point of recruitment.

iii) Anyone not capable of giving informed consent.

iv) Non-English proficient.

v) Score <3 on all PANSS positive, negative and general items.

## 2. Outcome measures

### Primary outcome

The primary outcome is psychotic symptoms measured by PANSS total score at 12 weeks post randomisation(1).

### Secondary outcomes

At 24 weeks randomisation:

1. 1. Psychotic symptoms measured using PANSS total score (1)

At 12 weeks post randomisation and 24 weeks post randomisation:

1. Symptom distress measured using:
  - i. Psychotic Symptoms Rating Scales (PSYRATS) delusions subscale (2)
  - ii. PSYRATS hallucinations subscale (2)
2. Mood measured using the Calgary Depression Scale (CDSS) for Schizophrenia (3)
3. Social functioning measured using the Personal and Social Performance Scale total score (PSP) (4)
4. Perceived criticism and warmth measured using:
  - i. Perceived Criticism and Perceived Warmth Scale (PCPW) perceived criticism subscale (5)
  - ii. PCPW perceived warmth subscale (5)
5. Recovery is measured using the Questionnaire about the Process of Recovery (QPR) (6)
6. Well-being is measured using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWEBS) (7, 8)
7. Internalised stigma is measured using the Internalised Stigma of Mental Illness Inventory (ISMI) (9)
8. Substance use measured using:
  - i. The Alcohol Use Disorders Inventory (AUDIT; past 3 months) (10, 11)
  - ii. Cannabis Use Disorders Inventory-Revised (CUDIT-R; past 3 months) (12)
  - iii. Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (13)
    - Separate scores for: tobacco, alcohol, cannabis, cocaine, amphetamine type simulants, inhalants, sedatives, hallucinogens, opioids, and other drugs
  - iv. Three subscales of the Drug Use Disorder Identification Test-Extended - cannabis only (DUDIT-e) (14):
    - Positive aspects
    - Negative aspects
    - Treatment readiness
  - v. Cannabis use in the last month, and last 3 months measured using the Time Line Follow Back for drugs and alcohol (TLFB). We will analyse two outcomes from this data (15, 16):
    - Proportion of days using cannabis
    - Average daily weight per cannabis using day
9. Empowerment is measured using the Empowerment Scale (ERS) (17)

### **App Engagement**

1. App engagement is measured at 12 weeks using the Quantitative Feedback Questionnaire (QFQ) aggregated into four subscales:
  - i. Ease of use
  - ii. Fit in daily life
  - iii. Acceptability
  - iv. Perceived helpfulness

### **Health economic outcomes**

1. Quality of life measured using Euro-Qol Five Dimension (EQ-5D-5L)  
Service utilisation, income, accommodation and other cost-related variables measured using the Client Service Receipt Inventory (CSRI).

## **3. General analysis principles**

We will report data in line with the Consolidated Standards of Reporting Trials (CONSORT) 2018 Statement for Social and Psychological Interventions showing attrition rates and loss to follow-up (see CONSORT diagram, appendix 3).

Analysis will be carried out using the intention to treat principle: participants analysed in the group they are randomised to, and available data from all participants is included, including those who do not complete therapy (18). Every effort will be made to follow up all participants in both arms for research assessments.

Analysis of outcomes relating to cannabis use only will be carried out on the subpopulation of the trial that are cannabis users at baseline. This will apply to CUDIT-R, DUDIT-E (all subscales), and outcomes derived from the TLFB for cannabis for both one month and three month recall: proportion of using days and average daily weight per using day. People will be classified as cannabis users at baseline if they answer “never” to item one of CUDIT-R: “How often do you use cannabis”.

This statistical analysis plan will be agreed with the trial steering committee before any inspection of post-randomisation data by the research team. No interim analysis is planned.

Analysis will be conducted in Stata version 16.0 or later.



#### **4. Data summary and reporting**

Descriptive statistics within each randomised group will be presented for baseline values. These will include counts and percentages for binary and categorical variables, and means and standard deviations, or medians with lower and upper quartiles, for continuous variables, along with counts of missing values. There will be no tests of statistical significance or confidence intervals for differences between randomised groups on any baseline variable.

Descriptive statistics will be used to summarize drop-out and completeness of therapy.

Outcomes at 12 and 24 weeks will be presented separately for each group and summarised using means and standard deviations, along with counts of missing values.

The number of serious adverse events and adverse events will be presented as the number of events and number of individuals with events. These will be provided separately for each randomised group.

## **5. Statistical methods for inferential analysis**

### **Analysis of primary and secondary outcomes**

The primary and secondary outcomes, with the exception of the proportion of cannabis free days, will be analysed using a linear mixed-effects models with outcome measurement (at the two follow-up time points) as the dependant variable. The model will include fixed effects for timepoint, treatment, timepoint by treatment interactions, the baseline measure of the outcome, assuming a linear relationship between baseline and outcome, and service (2 categories: i) early intervention; ii) community mental health). Observations will be clustered by participant with an unstructured correlation matrix for the residuals. The model will be fitted using restricted maximum likelihood (19).

For each outcome and timepoint we will report the treatment effect estimate as the adjusted mean difference between groups, its standard error, 95% confidence intervals and p-value.

In addition, we will report estimates for Cohen's D effect sizes as the adjusted mean difference of the outcome divided by the sample standard deviation of the outcome at baseline. Confidence intervals for Cohen's D will be calculated by dividing the confidence limits by the sample standard deviation of the outcome at baseline. These will be displayed in a Forest Plot with the primary outcome at the top, followed by secondary outcomes.

### **Time line follow back (TLFB)**

Average weight per using day will be analysed using a linear mixed-effects model in the same way as other primary and secondary outcomes.

The proportion of cannabis free days will be analysed using a mixed effects generalised linear model, with family binomial and an identity link. The random and fixed parts of the model will be specified in the same way as the mixed effects model for other primary and secondary outcomes, including the baseline proportion of cannabis free days as a fixed effect.

Inferential analysis will only be conducted on outcomes from the TLFB separately for one month recall and three month recall (proportion of abstinent days and Average daily weight per cannabis using day).

### **ASSIST**

The ASSIST will not be included in the inferential analysis of primary and secondary outcomes and instead summarised using descriptive statistics. For each substance, the total score for ASSIST will be summarised using mean and standard deviation by randomised group and timepoint.

### **Analysis of app engagement**

We will report means and standard deviations by group for each of the four subscales of the QFQ: a) Ease of use b) Fit in daily life c) Acceptability, and d) Perceived helpfulness.

### **Analysis of health economic outcomes**

The visual analogue scale from the EQ-5D-L will be analysed using a mixed effects model implemented in the same way as for the analysis of clinical outcomes. The five components for the EQ-5D-L will be summarised by treatment group and time point using the mean and standard deviation.

The CSRI will be summarised using descriptive statistics only. We will present the number and proportion of participants at each time point who have had:

- i. Hospital inpatient stay (at least overnight)
- ii. Outpatient appointment (4 hours or less)
- iii. Day appointment > 4 hours
- iv. Use of A&E

Other data collected as part of the CSRI will not be summarised as part of this analysis.

### **Missing data**

#### Imputation and pro-rating

Missing data on individual measures will be pro-rated on a subscale level if more than 90% of the items of a subscale are completed; otherwise the measure will be considered as missing. Exceptions where this rule does not apply for PANSS and ISMI are given below. Missing values in baseline covariates will be handled using mean imputation – the missing value will be imputed with the mean of the covariate for all participants in the trial (20).

When follow up of PANSS was completed over the phone, item one on the negative subscale (N1) and 4 and 5 on the general subscale (G4, G5) were not completed as these items are based on observation. Where these items are missing, they will be prorated as the mean of the respective subscale. When this occurs no additional items will be prorated – if in addition to N1, G4, and G5 have not been completed the measure will be considered missing.

The questionnaire instructions for ISMI define the total score for the outcome as the mean of all completed items. For this scale we will calculate a score if any items have been completed.

#### Assumptions for primary analysis

The primary analysis assumes data are missing at random, conditional on the observed values of the outcome at baseline, and follow up, and other covariates in the model.

#### Sensitivity analysis

We will conduct a sensitivity analysis for the primary outcome to assess whether different assumptions about missing data lead to different results. The sensitivity analysis will be conducted using the same model as is used in the primary analysis with the addition of baseline variables found to be predictive of missingness. Baseline variables will be considered predictive of missingness if  $p < 0.05$  in a univariate logistic regression model, with attending the visit as the outcome and the baseline variable of interest as the only predictor. This sensitivity analysis will assume data is missing at random conditional on the variables in the primary analysis model and variables that are found to be predictive of missingness.

### **COVID-19 pandemic**

In light of the COVID-19 pandemic and the actions to mitigate the spread of the coronavirus, these actions may have an effect on the data collected in the Actissist 2.0 trial from March 2020 onwards. Recruitment had ceased by this date and all 12 week follow-ups had been completed. Therefore, the only data that could feasibly be impacted by the COVID-19 actions are the 24 week outcome measures of the remaining 21 participants.

We will perform an independent samples t-test comparing the 24 week PANSS outcome between the participants whose PANSS was collected before 1<sup>st</sup> March 2020, and those participants collected after 1<sup>st</sup> March 2020. If there are significant differences in the mean scores, we will conduct a sensitivity analysis for the intention-to-treat analysis by excluding participants with 24 week follow-ups collected after 1<sup>st</sup> March 2020.

### **Accounting for versions of Actissist**

Digital interventions are characterised by the iterative changes to the interventions during the life of a trial. As the app is updated to a new version, participants in the Actissist arm will receive a newer version of the app if they are recruited later in the study. ClinTouch remained unchanged during the duration of the study. For the intention-to-treat analysis, we ignore the version of the app and compare Actissist versus ClinTouch based on random assignment. Therefore, this analysis necessarily averages over different versions of the intervention.

Since the app version is only available in the intervention arm of the trial, simple covariate adjustment for app-version is not recommended. Instead, we consider categorical time periods during recruitment to the study, which serves as a proxy for the version of the Actissist app that was available at the time of randomisation. This indicates the version of the Actissist app that participants randomised to the Actissist arm received, and the version that the ClinTouch arm would have received had they been randomised differently. This is measured at baseline in all participants regardless of subsequent random assignment.

As a subgroup analysis, we will repeat the primary analysis in subgroups defined by each time period of recruitment. We will test if the treatment effect is equal across time periods, and interpret differences to be indicative of the version of the app available at that time period.

## 6. References

1. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull.* 1987;13(2):261-76.
2. Haddock G, McCarron J, Tarrier N, Faragher EB. Scales to measure dimensions of hallucinations and delusions: the psychotic symptom rating scales (PSYRATS). *Psychol Med.* 1999;29(4):879-89.
3. Addington D, Addington J, Maticka-tyndale E. Assessing Depression in Schizophrenia: The Calgary Depression Scale. *Br J Psychiatry.* 1993;163(S22):39-44.
4. Patrick DL, Burns T, Morosini P, Rothman M, Gagnon DD, Wild D, et al. Reliability, validity and ability to detect change of the clinician-rated Personal and Social Performance scale in patients with acute symptoms of schizophrenia. *Curr Med Res Opin.* 2009;25(2):325-38.
5. Schlosser DA, Zinberg JL, Loewy RL, Casey-Cannon S, O'Brien MP, Bearden CE, et al. Predicting the longitudinal effects of the family environment on prodromal symptoms and functioning in patients at-risk for psychosis. *Schizophr Res.* 2010;118(1-3):69-75.
6. Law H, Neil ST, Dunn G, Morrison AP. Psychometric properties of the questionnaire about the process of recovery (QPR). *Schizophr Res.* 2014;156(2-3):184-9.
7. Bass M, Dawkin M, Muncer S, Vigurs S, Bostock J. Validation of Warwick-Edinburgh Mental Well-being Scale (WEMWBS) in a population of people using Secondary Care Mental Health Services. *J Ment Health.* 2016;25(4):323-9.
8. Taggart F, Stewart-Brown S, Parkinson J. Warwick-Edinburgh Mental Well-being Scale (WEMWBS) - User guide – Version 2. In: Scotland NH, editor. 2015.
9. Ritsher JB, Otilingam PG, Grajales M. Internalized stigma of mental illness: psychometric properties of a new measure. *Psychiatry Res.* 2003;121(1):31-49.
10. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. The Alcohol Use Disorders Identification Test -Guidelines for Use in Primary Care Second Edition. In: World Health Organization DoMHaSD, editor. 2001.
11. Cassidy CM, Schmitz N, Malla A. Validation of the Alcohol Use Disorders Identification Test and the Drug Abuse Screening Test in First Episode Psychosis. *Can J Psychiatry.* 2007.
12. Bonn-Miller MO, Heinz AJ, Smith EV, Bruno R, Adamson S. Preliminary Development of a Brief Cannabis Use Disorder Screening Tool: The Cannabis Use Disorder Identification Test Short-Form. *Cannabis Cannabinoid Res.* 2016;1(1):252-61.
13. Humeniuk R, Henry-Edwards S, Ali R, Poznyak V, Monteiro M, G. M. The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) Manual for use in primary care World Health Organisation; 2010.
14. Berman AH, Palmstierna T, Kallmen H, Bergman H. The self-report Drug Use Disorders Identification Test: Extended (DUDIT-E): reliability, validity, and motivational index. *J Subst Abuse Treat.* 2007;32(4):357-69.
15. Barrowclough C, Gregg L, Lobban F, Bucci S, Emsley R. The impact of cannabis use on clinical outcomes in recent onset psychosis. *Schizophr Bull.* 2015;41(2):382-90.
16. Barrowclough C, Eisner E, Bucci S, Emsley R, Wykes T. The impact of alcohol on clinical outcomes in established psychosis: a longitudinal study. *Addiction.* 2014;109(8):1297-305.
17. Rogers ES, Chamberlin J, Ellison ML, Crean T. A consumer-constructed scale to measure empowerment among users of mental health services. *Psychiatr Serv.* 1997;48(8):1042-7.
18. White IR, Horton NJ, Carpenter J, Pocock SJ. Strategy for intention to treat analysis in randomised trials with missing outcome data. *Bmj-British Medical Journal.* 2011;342.
19. Rabe-Hesketh S, Skrondal A. Multilevel and longitudinal modeling using Stata. 3rd ed. College Station, Tex.: Stata Press Publication; 2012.
20. White IR, Thompson SG. Adjusting for partially missing baseline measurements in randomized trials. *Stat Med.* 2005;24(7):993-1007.

## Appendix 1 Example analysis code

Data will be in long format with two rows for each participant, one for 12 week time point and one row for the 24 week timepoint.

### Variable names

- pid: participant id
- treat: Arm of the trial participant is randomised to
- timepoint: follow-up timepoint
- baseline: baseline measure of the outcome
- service: Stratification factor
- outcome: outcome measure

### Analysis code

*\*Model for outcomes analysed using mixed effect model:*

```
mixed outcome i.treat##i.timepoint baseline service || pid:, ///  
res(unstructured, t(timepoint)) noconstant reml  
  
margins treat, at(timepoint==12) pwcompare(effects)
```

*\*Model for proportion of abstinent days from timeline follow back:*

```
meglm outcome i.treat##i.timepoint baseline service || pid:, ///  
res(unstructured, t(timepoint)) noconstant ///  
family(binomial 30) link(identity)
```

*\*\*End of treatment - should be the same as main effect of treat in above command*

*\*\*Follow-up*

```
margins treat, at(timepoint==24) pwcompare(effects)
```

*//Should be the same as main effect of treat in:*

```
// mixed outcome i.treat##ib24.timepoint baseline service || pid:, ///  
res(unstructured, t(timepoint)) noconstant reml
```

## Appendix 2: Deriving outcomes

### Scoring rules for outcomes

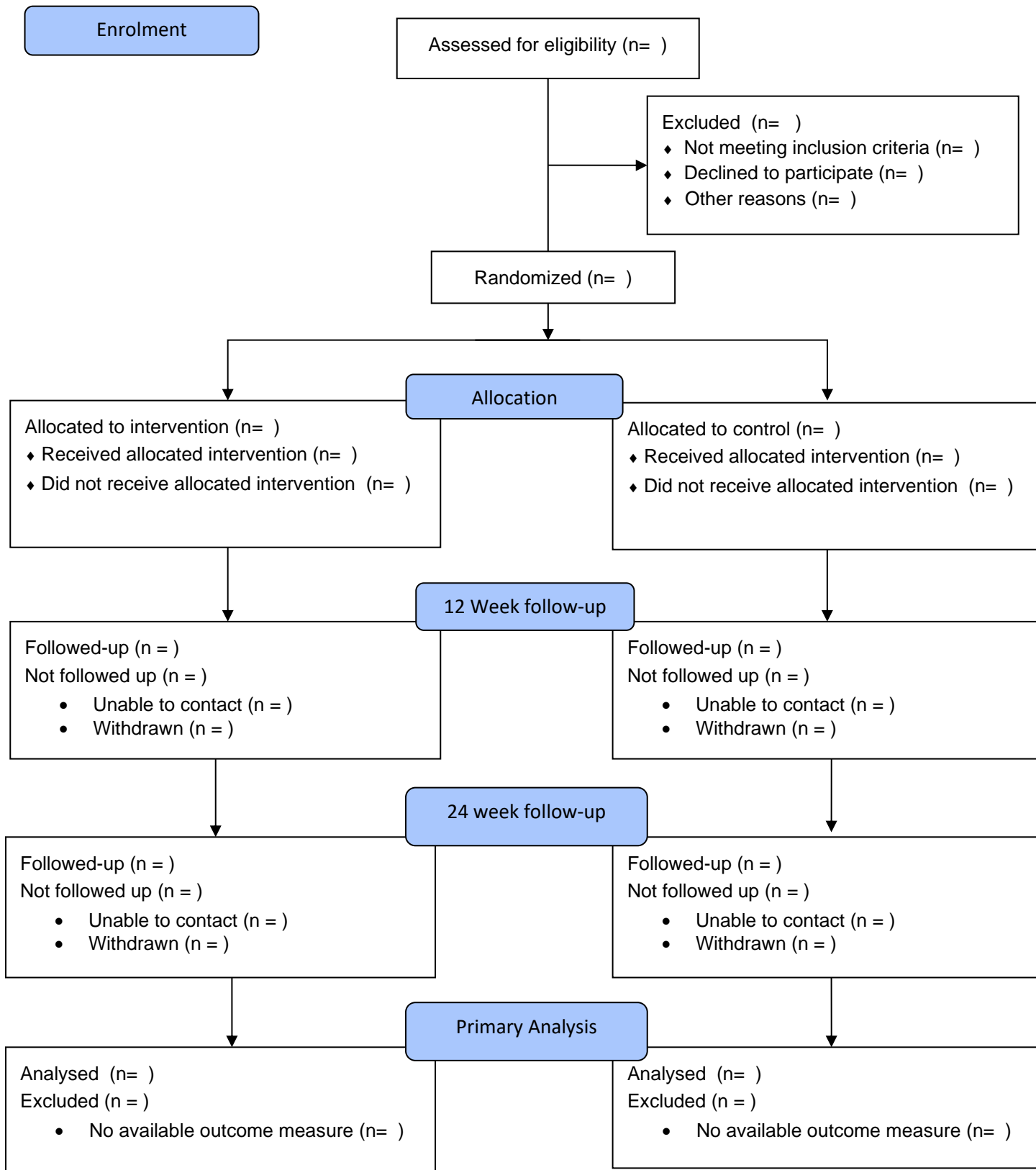
| Outcome acronym                           | Number of questions           | Scoring                                                                 | Min-Max possible values           | Scores for better outcomes  |
|-------------------------------------------|-------------------------------|-------------------------------------------------------------------------|-----------------------------------|-----------------------------|
| PANSS total score                         | 30 (7 +ve, 7 -ve, 16 general) | Sum of items                                                            | 30-210                            | Lower                       |
| PSYRATS - delusions                       | 6                             | Sum of all items                                                        | 0-24                              | Lower                       |
| PSYRATS - hallucination                   | 11                            | Sum of all items                                                        | 00-44                             | Lower                       |
| CDSS                                      | 9                             | Sum of items                                                            | 0-27                              | Lower                       |
| PSP                                       | 4                             | Total score is entered directly into the database                       | 1-100                             | Higher                      |
| PCPW – Perceived criticism                | 4                             | Mean of items                                                           | 1-10                              | Lower                       |
| PCPW – Perceived warmth                   | 3                             | Mean of items                                                           | 1-10                              | Lower                       |
| QPR                                       | 15                            | Sum of the items                                                        | 15-75                             | Higher                      |
| WEMWEBS                                   | 14                            | Sum of the items                                                        | 14-70                             | Higher                      |
| ISMI                                      | 29                            | Mean of completed items reverse scoring items 7, 14, 24, 26 and 27      | 1-4                               | Lower                       |
| AUDIT; past 3 months)                     | 10                            | Sum of items                                                            | 0-40                              | Lower                       |
| CUDIT-R; past 3 months.                   | 8                             | Sum of items                                                            | 0-32                              | Lower                       |
| ASSIST                                    | 71                            | Sum of items by substance.                                              | 0-31 tobacco<br>00-39 other drugs | Lower                       |
| DUDIT-e: Positive aspects                 | 17                            | Sum of items                                                            | 0-68                              | Higher scores more positive |
| DUDIT-e: Negative aspects                 | 17                            | Sum of items                                                            | 0-68                              | Higher scores more negative |
| DUDIT-e: Treatment readiness              | 8                             | Sum of items excluding items 6 and 7 and reverse scoring items 1 and 9. | 0-16                              | Higher scores more ready    |
| TLFB – Proportion of days using cannabis* | 1                             | Numerator: 30 – number of days abstinent<br>Denominator: 30             | 0-1                               | Lower                       |

|                                                     |    |                                                                                                                                                              |              |        |
|-----------------------------------------------------|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|--------|
|                                                     |    |                                                                                                                                                              |              |        |
| TLFB - Average daily weight per cannabis using day* | 2  | Total weight/using days.<br>Total weight = number of units consumed.<br>Using days = (30 – number of days abstinent)<br>If using days = 0 outcome will be 0. | Non-negative |        |
| ERS                                                 | 28 | Sum of the items. Reverse score items 10-18, and item 28.                                                                                                    | 28-112       | Higher |
| QFQ - Ease of use                                   | 5  | Qs 7, 8 (reversed), 11, 12 (reversed)                                                                                                                        | 1-7          | Lower  |
| QFQ - Fit in daily life                             | 5  | Qs 3, 5, 6, 9, 10, and 21                                                                                                                                    | 1-7          | Lower  |
| QFQ - Acceptability                                 | 6  | Qs 4, 15, 16, 17 (reversed), 20, 22 (reversed)                                                                                                               | 1-7          | Lower  |
| QFQ - Perceived helpfulness                         | 4  | Qs 13 (reversed), 14 (reversed), 18 and 19 (reversed)                                                                                                        | 1-7          | Lower  |

\*One month recall data was collected using a 30 day period. For three month the time period was 90 days.



### Appendix 3: CONSORT diagram



**Appendix 4: Draft tables**

**Table XX: Primary and secondary outcomes**

|          | Unadjusted, Mean (SD)     |                           |                                               |                            |
|----------|---------------------------|---------------------------|-----------------------------------------------|----------------------------|
| Outcome  | ACTISSIST<br><i>n= XX</i> | ClinTouch<br><i>n= XX</i> | Adjusted Difference (SE);<br>p-value (95% CI) | Cohen <i>d</i><br>(95% CI) |
| Outcome  |                           |                           |                                               |                            |
| Baseline |                           |                           | -                                             | -                          |
| 12 weeks |                           |                           |                                               |                            |
| 24 weeks |                           |                           |                                               |                            |