# Acne Care Online: Statistical analysis plan for a randomised trial of a digital behaviour change intervention to improve acne-related quality of life amongst 13-25 year olds

| | |
|---|---|
| **Trial name:** | Acne Care Online (ACO) |
| **Trial registration number:** | https://www.isrctn.com/ISRCTN65493744 |
| **Protocol title and version number:** | Acne Care Online: feasibility and full-scale RCT of an online intervention to support acne self-management Protocol v3 04 Feb 2025 |
| **SAP version number:** | 1.0 |
| **SAP date:** | 23 October 2026 |

**To be approved and reviewed by:**

| | Name | Signature | Date |
|---|---|---|---|
| **Chief Investigator** | Professor Miriam Santer |  | 21/10/2026 |
| **Trial Statistician (author)** | Dr Taeko Becque |  | 14/10/2026 |
| **Senior Statistician (review)** | Professor Beth Stuart |  | 21/10/2026 |

# 1. Purpose of the SAP

The Statistical Analysis Plan (SAP) provides a comprehensive and detailed description of the methods and presentation of data analyses proposed for the “Acne Care Online (ACO)” trial.

The purpose of the plan is to:

1. Ensure that the analysis is appropriate for the aims of the trial, reflects good statistical practice, and that interpretation of a priori and post hoc analyses is appropriate.
2. Explain in detail how the data will be handled and analysed to enable others to perform the actual analysis in the event of sickness or other absence.

Additional exploratory or auxiliary analyses of data not specified in the protocol are permitted but fall outside the scope of this SAP (although such analyses would be expected to follow Good Statistical Practice).

The statistical analysis plan will be made available if required by journal editors or referees when the main papers are submitted for publication. Additional analyses suggested by reviewers or editors will, if considered appropriate, be performed in accordance with the SAP, but if reported the source of such a post-hoc analysis will be declared.

Amendments to the statistical analysis plan will be described and justified in the final report of the trial.

# 2. Study Design

## 2.0 Trial background and rationale (short synopsis from trial registration)

Acne is very common, frequently causes distress or low self-confidence, and may lead to permanent scarring, long-lasting dark marks, or depression. Treatment of acne is a major cause of antibiotic use amongst young people, leading to antibiotic resistance. Evidence and guidelines suggest that topical treatments (creams or gels applied directly to the skin) should be the main treatments for acne.

Acne vulgaris (hereon acne) is very common, affecting over 90% of teenagers, and commonly persisting into adulthood.(1) Acne can cause decreased self-confidence, increased rates of depression and suicidal ideation.(2) Acne is thought to cause scarring in approximately 20% of the population.(2) As well as limiting quality of life, acne is a major cause of antibiotic use, with one study demonstrating that long-term prescribing of antibiotics commonly used for acne account for 72% of total antibiotic days amongst people aged 11 to 21 years.(3) Antibiotic resistance arising from acne treatment is an increasing concern with use of effective alternatives to antibiotics being a major priority.(4) Health service use for acne is substantial with 3% of people aged 13-25 visiting their GP for acne each year, of whom 8% are referred to secondary care.(5)

Effective topical treatments are available from pharmacies without a prescription, but many people are unaware of these and buy cosmetic products that don't help instead.(6) People often give up on topical treatments because they are not given full advice on how to use them. (6) We have developed Acne Care Online, a new website to help young people to manage acne more effectively, including information on how to obtain effective treatments, promote regular treatment use and advice on how to avoid side effects

## 2.1. Trial aims and objectives

Aim
To assess whether Acne Care Online website improves outcomes for people with acne and reduces the use of long-term oral antibiotics.

Objectives
To determine the effectiveness of the Acne Care Online behavioural intervention in improving acne-related quality of life compared to standard care in a randomised trial, with antibiotic use and service use as important secondary outcomes.

## 2.2. Trial design and configuration

A multi-centre individually randomised trial with internal pilot, nested health economic evaluations and mixed-methods process evaluation studies. This full-scale trial follows a previous feasibility study, which met all progression criteria with no substantial changes to intervention or study processes so in effect became the internal pilot of the full-scale trial.

## 2.3. Trial centres

Recruitment is through primary care, community pharmacies, schools and colleges, community advertising as well as social media. General practice recruitment is through East Midlands RRDN (formerly East Midlands CRN), East of England (formerly Kent, Surrey and Sussex CRN), North East and North Cumbria (formerly North East and North Cumbria CRN), North West London (formerly North West London CRN), North West (formerly North West Coast CRN), South Central (formerly Wessex CRN & Thames Valley and South Midlands CRN), South West Central (formerly West of England CRN), South West Peninsular, West Midlands (formerly West Midlands CRN), Yorkshire & Humber (formerly Yorkshire & Humber CRN), Hampshire & Isle of Wight NHS Foundation Trust (was Solent NHS Trust).

***Opportunistic recruitment in pharmacies***

Potential participants, or their parent/carer if under 16, were given a link directing them to the study website via advertisement on screens (16-25 only) or by summary participant information sheet given by the pharmacy professional. The study website included a full participant information sheet, who to contact for further information or discussion, information on eligibility and how to proceed to provide online consent prior to participating in study activities.

***Recruitment through schools/colleges***

We engaged with teaching, pastoral or school nursing staff to raise awareness of the research, including the possibility of research participation and how to take part. This included invitations to take part in the study via letter, SMS text or email from the school or college directing interested individuals to the study website. All potential participants invited via this route were contacted initially via their parent/carer given that many were likely to be under the age of 16.

***Community or social media advertising***

Community or social media advertising was targeted at potential participants aged 16 or over. Posters were displayed in locations such as GP surgeries, community pharmacies, post-16 education colleges, and social media. Posters invited potential participants, directing them towards the study website, which included full participant information, who to contact for further information or discussion, information on eligibility and how to proceed to provide online consent prior to participating in study activities.

## 2.4. Eligibility criteria

### 2.4.1. Inclusion criteria

Participants were eligible for inclusion if:

- They were aged 13-25 years with self-defined acne with current active lesions (i.e. mild or worse on self-assessment scale)
- They had internet access

### 2.4.2. Exclusion criteria

Potential participants were excluded if:

- Their acne was clear or almost clear, i.e. if they answer 'no' to the following question asked online at baseline screening: *"Do you have spots or acne on your face at the moment? This could include whiteheads or more red spots or bumps."*
- They were unable to give informed consent or their parent didn't provide consent (for participants aged 13-15 recruited via community or social media advertising)
- They were unable to read and write English as the intervention content and outcome measures were in English
- They were currently taking oral isotretinoin or had taken it within the previous 3 months, as advice about topical acne treatments may be inappropriate in this case
- They took part in interviews as part of Acne Care Online intervention development. (Qualitative interviewees who did not view intervention materials were NOT excluded)
- Only one person per household could take part in the study.

## 2.5. Description of interventions

Participants were randomised 1:1 to either:

**Intervention Group**
Participants randomised to the intervention group were given access to the Acne Care Online behavioural intervention to support effective acne self-management, in addition to usual care.

**Control Group**
Participants randomised to the control group were signposted to the NHS advice page on acne, in addition to usual care.

Participants in both groups continued to receive their usual medical advice provided by their GP surgery and other healthcare services, including prescriptions or self-management including over-the-counter medications, and any online information that they wished to use. Both groups were given access to the Acne Care Online website after completing their 12-month study period.

## 2.6. Randomisation procedures

Participants completed informed consent/assent and baseline questionnaires online within LifeGuide+ software. Eligible participants were then randomised to the intervention group or control group by the software. Randomisation was carried out in a 1:1 ratio in blocks of 4 and 6 and stratified by gender, age at sign-up (13 to 15 years vs. 16 to 25 years) and recruitment source (general practice vs. social media/pharmacy/schools/colleges/community recruitment).

## 2.7. Sample size and justification

**Original target sample size**

Based on comparison of the Acne-QoL symptoms subscale at 12 weeks, power 90%, alpha 0.05 and seeking a standardised effect size of 0.30 (standard deviation 5.8), 470 participants were needed. Allowing for 20% loss to follow up gave a total 588 participants (294 per group). An effect size of

0.30 equates to a difference in Acne-QoL symptoms subscale between groups of 1.74 points, meaning we would be conservatively powered to detect the published minimal clinically reported difference for Acne-QoL, which is a difference of 2 points on the symptom subscale.(7, 8) A standard deviation 5.8 aligns with trials with a similar patient group.(8) Based on recruitment to the SAFA trial (HTA16/13/02) this sample size was deemed to be achievable in the proposed timescale. More information on scoring of the Acne-QoL is given below.

**Updated target sample size**

Due to lower than anticipated engagement with the intervention (72% rather than 80%), we increased our target sample size as follows. Based on comparison of the Acne-QoL symptoms subscale at 12 weeks, power 90%, alpha 0.05, mean difference 2 points and standard deviation 5.8, 356 participants were needed. Allowing for 30% nonadherence would require 356/0.7^2=727, and allowing for 20% loss to follow up requires 908 participants in total (ethics amendment 4, 04/02/2025).

## 2.8. Blinding

Blinding of participants was not possible. Following randomisation, participants were immediately informed online to which group they were allocated. It is not possible for all members of the study team to remain masked to treatment allocation, particularly those carrying out process evaluation interviews and those assisting with identifying participants for process evaluation interviews. The trial statisticians will remain masked to treatment allocation until all analysis code has been written and checked.

## 2.9 Contamination

Acne Care Online intervention was only accessible via sign-up link and subsequently login tied to a specific email address, during the period of the trial. Therefore, it would not have been possible for participants in the control group to access the intervention, until after 12 month follow up completed. It is possible that participants in the intervention group could have taken screen shots of the intervention and shared them, but unlikely that participants would know each other. Invitation into the study was limited to one person per household to minimise this risk.

## 2.10. Feasibility trial and internal pilot

The analysis of the feasibility study focused on recruitment and retention rates, participant characteristics (to ensure a diverse sample), missing data, acceptability of outcome measures and intervention usage. As no substantial changes to intervention or questionnaires were needed then data from feasibility trial participants became the internal pilot trial. The internal pilot phase comprised the first 85 participants and was assessed according to progression criteria (including that recruitment exceeded 70% of predicted). Therefore, no substantial changes to recruitment were needed and the internal pilot was rolled into a full-scale trial following a discussion with the Programme Management Group and Programme Steering Committee. Data from these participants will contribute to the full-scale trial analyses.

## 2.11. Timing of planned analyses

### Interim analyses

No interim analysis was planned.

### Final analysis

Final analysis will take place after all recruited participants have completed 52-week follow up, or received at least 3 reminders to do so. End of study is defined as when the last participant has had their last data collected, cleaned and verified.

# 3. General Analysis Considerations

## 3.1. Definition of analysis populations

Data will be reported and presented according to the revised CONSORT (Consolidated Standards of Reporting Trials) Statement.

The primary estimand of interest will be the treatment policy estimand. The intention-to-treat population will include all randomised participants according to randomised group. Missing data will be imputed as set out below and sensitivity analyses will explore the effect of missing data, as below.

We will undertake a complier-average causal effect analysis which compares compliant participants in the intervention group, with those in the control group whose characteristics are similar enough to the intervention group compliers to suggest they too would have complied with the intervention, given the opportunity to do so.

Adherence for these analyses will be defined as meeting minimum meaningful engagement with the online intervention (the point at which it is possible for participants to receive any of the key advice / recommendations / information) i.e. participants progressing at least one page beyond the 'dashboard' page where they received tailored recommendations about which elements of Acne Care Online to view.

## 3.2. Procedures for handling data

### 3.2.1 Withdrawal from trial

All data up until the point of participant withdrawal from the trial will be used in analyses unless the participant withdrew consent and does not wish for the data already collected prior to withdrawal to be used for the trial.

### 3.2.2 Missing data

For missing items within the Acne-QoL questionnaire, the guidance from the scoring manual will be followed.(7, 8) If a patient has a partially completed domain (minimum 3 items completed, or 1-2 questions have missing responses), we will calculate the mean value within the domain for the answered items and replace missing values with the mean value. If more than this minimum is missing, then the domain score will be missing. For all other outcome measures, missing items will be treated as missing, in accordance with the scoring guidelines.

The primary outcome will be analysed using complete data. However, the frequency and pattern of missing data will be examined and, if appropriate we will undertake a sensitivity analysis using multiple imputation with chained equations, assuming that the data are missing at random (MAR). The imputation model will include all variables in the analysis model and auxiliary variables that predict missingness of the outcome. We will include sensitivity analyses using delta-based multiple imputation to explore the impact of data missing not at random (MNAR),.

### 3.2.3 Outliers

No methods will be used to handle outliers in the data.

### 3.2.4 Assumption checking and alternative methods

Assumptions for linear regressions will be checked using quantile-quantile (Q-Q) plots for normality and residual vs fitted value plots for linearity and homoscedasticity. If linear modelling assumptions are not met, the data may be transformed using, e.g., a Box Cox transformation, and back transformed at values of interest. Alternatively, generalised linear mixed models may be used, e.g., Poisson mixed model with robust standard errors.

### 3.2.5 Online data entry vs data collected by telephone

Non-responders to questionnaire reminders are followed up by telephone and, where possible, missing data is collected by telephone. Where some data has been entered by the participant online within LifeGuide+ before or after this telephone call the online data will be used. Where online data is missing then telephone data will be used.

## 3.3. Definition of key derived variables

#### Acne-QoL symptom subscale

**The primary endpoint** is the Acne-QoL[2,3] symptom subscale score at 12 weeks. (Questionnaire invitation is sent at 12 weeks with follow-up window up to 6 weeks beyond this date). The Acne-QoL symptom subscale is calculated from the total of the 5 questions from the acne symptoms domain of the Acne-QoL questionnaire by summing the items 15-19 (see Appendix 1).[6] The 5 questions are on a scale of 0-6 ("extensive, a whole lot, a lot, a moderate amount, some, very few, none" for items 15-17 and "extremely, very much, quite a bit, a good bit, somewhat, a little bit, and not at all." for items 18 and 19). Possible domain scores range from 0 to 30 (where 30 is most severe) and the MCID is considered to be 2 points.

#### Other Acne-QoL subscales (self-perception, role-emotional and role-social)

The three other domains of the Acne-QoL are measured as secondary endpoints at 12, 24, 36 and 52 weeks. Each domain consists of the questions measured on a scale of 0-6 (extremely, very much, quite a bit, a good bit, somewhat, a little bit, and not at all). Possible domain scores range from 0 to 30.

- Self-perception Acne-QoL symptom subscale score is calculated from the total of the 5 questions from the Acne- QoL questionnaire by summing items 1, 3, 10, 2, and 6. (7, 8)
- Role-emotional Acne- QoL symptom subscale score is calculated from the total of the 4 questions from the Acne- QoL questionnaire by summing items 11-14. (7, 8)
- Role-social Acne-QoL symptom subscale score is calculated from the total of the 5 questions from the Acne- QoL questionnaire by summing items 4, 5, 7, 8 and 9. (7, 8)

#### Total Acne-QoL

The total Acne-QoL score is calculated as the sum of all four subscales as defined above.

### Participant's global assessment of acne

Participant's Global Assessment is asked at baseline with responses on a 5 point scale. Potential participants are excluded if their acne is clear or almost clear in response to the following question: How would you describe the acne on your face at the moment: 0 (Clear; no blackheads or whiteheads, no red or dark bumps); 1 (Almost clear; very few blackheads or whiteheads, no more than one small red or dark bump); 2 (Mild; worse than 1, some blackheads or whiteheads, no more than a few red or dark bumps); 3 (Moderate; worse than 2, up to many blackheads or whiteheads and some red or dark bumps, but no more than one small bump under the skin); 4 (Severe; worse than 3, up to many blackheads or whiteheads and red or dark bumps, but no more than a few bumps under the skin)

### Problematic Experiences of Therapy Scale

Problematic Experiences of Therapy Scale (PETS)(9) will be asked prior to adherence questions at baseline, 12 weeks and 52 weeks. The PETS asks participants to what extent they had been prevented from carrying out the intervention by socially acceptable reasons in order to explore barriers to adherence and promote reporting of non-adherence (e.g. "Lack of time prevented me from carrying out the treatment"). The scale comprises 12 items divided into four subscales: ''symptoms too severe or aggravated by therapy'' (items 1–3), ''uncertainty about how to carry out the treatment'' (items 4–5), ''doubts about treatment efficacy'' (items 6–8), and ''practical problems'' such as lack of time or opportunity, forgetting (items 9–12). All items are scored on a scale ranging from 1 (disagree strongly) to 5 (agree strongly). The scores will be recoded into binary categories as follows: participants who respond ''strongly disagree'' to all items in a subscale are recoded as ''no barriers'', and all other scores are recoded as ''some barriers or doubts''. For each subscale, the categories will be summarised descriptively by intervention arm.

### Patient Enablement Instrument

Patient Enablement Instrument (PEI)(10) will be measured at baseline, 12 weeks and 52 weeks to assess the extent to which usual care or intervention use has enabled participants to understand and self-manage their acne. The modified PEI asks 6 questions about the patients' ability to understand their problems and cope with illness. These are rated on a 7 point Likert scale (0=strongly agree to 7=strongly disagree). A mean overall score can be calculated, with lower scores equating to better enablement

### Brief Illness Perceptions Questionnaire

Brief Illness Perceptions Questionnaire (IPQ)(11) will be measured at baseline, 12 weeks and 52 weeks to explore participants beliefs about their acne that are expected to be important determinants of adherence to treatments (e.g. perceived impact, severity, control, treatability, timeline). There are 8 items scored on a 0-10 scale. To compute the score, reverse score items 3, 4, and 7 and add these to items 1, 2, 5, 6, and 8. A higher score reflects a more threatening view of the illness.

### PHQ-4

Patient Health Questionnaire (PHQ–4) for Anxiety and Depression(12) will be measured at baseline, 12 weeks and 52 weeks. The PHQ-4 is a 4-item measure of anxiety and depression. A total score of 3

or more for the first two questions suggests anxiety and a total score of 3 or more on the last two question suggestions depression.

### Oral antibiotic use and other acne treatment use

Participants are asked whether they are currently using oral acne treatments at baseline 12, 24, 36 and 52 weeks and, if yes, which type of treatment and since how many weeks they have been using this. One of the potential categories of treatments is 'antibiotics' and lists antibiotics commonly used to treat acne include oxytetracycline, tetracycline, lymecycline, doxycycline, erythromycin and trimethoprim. Antibiotic use will be treated as a binary (yes/no) variable at each timepoint.

Participants are asked about use of topical treatment for acne at baseline, 12 weeks, 24 weeks, 36 weeks and 52 weeks. If they are using topical treatments they are also asked about treatment adherence: over the last week, how often have you used them? Not at all / 1 to 3 times a week / 4 to 6 times a week / Once every day /More than once a day.

### Short Warwick Edinburgh Mental Well-being Scale (SWEMWBS)

The Short Warwick Edinburgh Mental Well-being Scale (SWEMWBS)(13) will be measured at baseline, 12 weeks, 24, 36 and 52 weeks. SWEMWBS is a seven-item measure of generic mental well-being and is both a secondary clinical outcome measure and a health economic outcome measure. The items are summed to create a total score.

### Other outcomes

Approach to Health Economic outcomes, such as the EQ-5D-5L and resource use will be detailed in the Health Economic Analysis Plan. Process evaluation analyses will also be described in a separate protocol.

## 3.4. General principles for reporting and analysis

- Summary statistics will consist of frequencies and percentages for categorical variables, means, ranges and standard deviations for normally-distributed continuous variables, and medians and inter-quartile ranges for continuous variables with a skewed distribution.
- One decimal place will be used for percentages, means, ranges, standard deviations, medians and inter-quartile ranges.
- Where multiple answers are provided, the percentages will reflect the number of each type of reported answers, where the denominator will be the number of answers obtained rather than the number of participants..
- Treatment group will be labelled in the tables as 'ACO Intervention' versus the control group labelled as 'Usual care'. Total column will be included in the tables as the last column.
- All tests will be two-tailed with point estimates, 95% confidence intervals and exact p-values for the treatment effect presented.
- Coefficients, p-values and 95% confidence intervals will be reported with two decimal points each in a separate column for the linear regression models.
- Odds ratios, p-values and 95% confidence intervals will be reported with two decimal points each in a separate column for the logistic regression models. The level of statistical significance will be taken at 5%.
- No formal adjustment for multiple significance testing will be applied.

# 4. Description of participant characteristics

## 4.1. Disposition

The flow of patients will be summarised in a CONSORT diagram (figure 1) that will include the numbers assessed for eligibility, reasons for exclusion, numbers randomised to the two treatment groups, numbers receiving the allocated intervention, losses to follow up and the numbers analysed.

## 4.2. Baseline characteristics

The baseline characteristics of the two groups with respect to gender, age, ethnicity, index of multiple deprivation (IMD) recruitment route, acne severity (baseline Acne-QoL symptoms), prior belief in effectiveness of online interventions for acne, duration of acne, current and past treatment use, adherence to topical acne treatments (if relevant) and quality of life (EQ-5D-5L, Short Warwick Edinburgh Mental Well-being Scale (SWEMWBS)) will be summarised.

Continuous data will be summarised in terms of the mean, standard deviation, and number of observations or, where skewed, median and lower & upper quartiles. Binary/categorical data will be summarised in terms of frequency counts and percentages.

# 5. Analysis of Effectiveness

## 5.1. Primary analysis

For the primary outcome, summary statistics will be presented for each group. A linear regression model will be used to analyse the between group difference in the Acne-QoL symptom subscale at 12 weeks. The model will be adjusted for randomisation stratification variables (gender, age and recruitment source)), baseline variables (including baseline Acne-QoL symptom subscale score). A 95% confidence interval for the least squares mean difference between arms in Acne-QoL symptom subscale at 12 weeks will be calculated. The frequency and pattern of missing data will be examined and a multiple imputation model will be used as a sensitivity analysis if appropriate, as set out in section 3.2.2 above.

A sensitivity CACE analysis will be carried out to explore the impact of adherence with the intervention. This will target a principal stratum estimand, focusing on the subpopulation of patients who would complete core sections of the intervention under either treatment assignment. The CACE analysis will be carried out using instrumental variables regression, with randomised group as the instrumental variable, and adherence defined above as the endogenous variable.

## 5.2. Analysis of secondary outcomes

The Acne-QoL symptom subscale score, as well as other three Acne-QoL subscales (self-perception, role-emotional and role-social) and the total score, will be analysed using the same approach as for the primary endpoint. These outcomes will also be described and the trend in the groups over time illustrated graphically.

As a secondary analysis we will also assess Acne-QoL symptom subscale and other Acne-QoL subscales with a repeated measures approach, using a multilevel mixed model allowing for observations (level 1) at all timepoints (12 weeks, 24 weeks, 36 weeks and 52 weeks) nested within participants (level 2) and adjusting for the same covariates as the primary analysis.

The PETS, PEI and IPQ will be treated as continuous measures and analysed using a linear regression model at 12 and 52 weeks.

The PHQ-4 will be treated as a binary outcome based on the thresholds set out in section 3.3 and analysed using logistic regression. Antibiotic use will be treated as a binary variable at 12 weeks and analysed using logistic regression. It will also be analysed using a repeated measures approach, across the 52 weeks follow-up period using a multilevel mixed model allowing for observations (level 1) at all timepoints (12 weeks, 24 weeks, 36 weeks and 52 weeks) nested within participants (level 2). The antibiotic treatments used will be summarised using descriptive statistics.

Use of topical treatment for acne, use of oral antibiotics for acne and use of other oral treatment for acne will be treated as binary outcomes and analysed using logistic regression. Adherence to topical acne treatments will be treated as a categorical outcome and analysed using ordinal logistic regression.

All results will be reported with 95% confidence intervals and all models will control for the baseline covariates set out in the primary analysis.

# 6. Analysis of Safety

## 6.1 Adverse events

No specific therapeutic intervention is proposed. This programme consists of online information to support acne self-management. We will not collect adverse events, but will assess for this possibility in process evaluation interviews.

# 7. Exploratory analysis

Although we are not powered to look at subgroups, we will explore the impact of key subgroups that could plausibly modify intervention effectiveness:

- Prior belief in the effectiveness of the intervention, i.e. response to the question 'How effective do you think a website might be in helping your acne: 1-3 relates to low belief; 4-6 moderate belief; and 7-9 high belief (3 categories)
- Severity of acne, i.e. baseline question, 'How would you describe the acne on your face at the moment?' Mild; Moderate; Severe (3 categories)
- Duration of acne, i.e. response to the question, 'How long have you had acne': Less than 6 months; 6 months or more but less than 2 years; 2 years or more but less than 5 years; 5 years or more (4 categories)
- Current/past treatment use with oral or topical treatments for acne – yes vs no
- Gender – Male vs Female
- Age – 13-15 vs 16+
- Ethnicity – "White" vs Ethnic minority
- Socioeconomic status – IMD <=5 vs >5.

For this exploratory analysis, estimates of the interaction between subgroup and intervention will be provided with 95% confidence intervals and the estimates of the intervention effect when the subgroup is selected. Clear evidence of benefit in a subgroup will require the interaction term for that subgroup to be significant at the 5% level. Although a formal adjustment for multiplicity will not be carried out, the results will be interpreted cautiously, as a significant result might arise by chance.

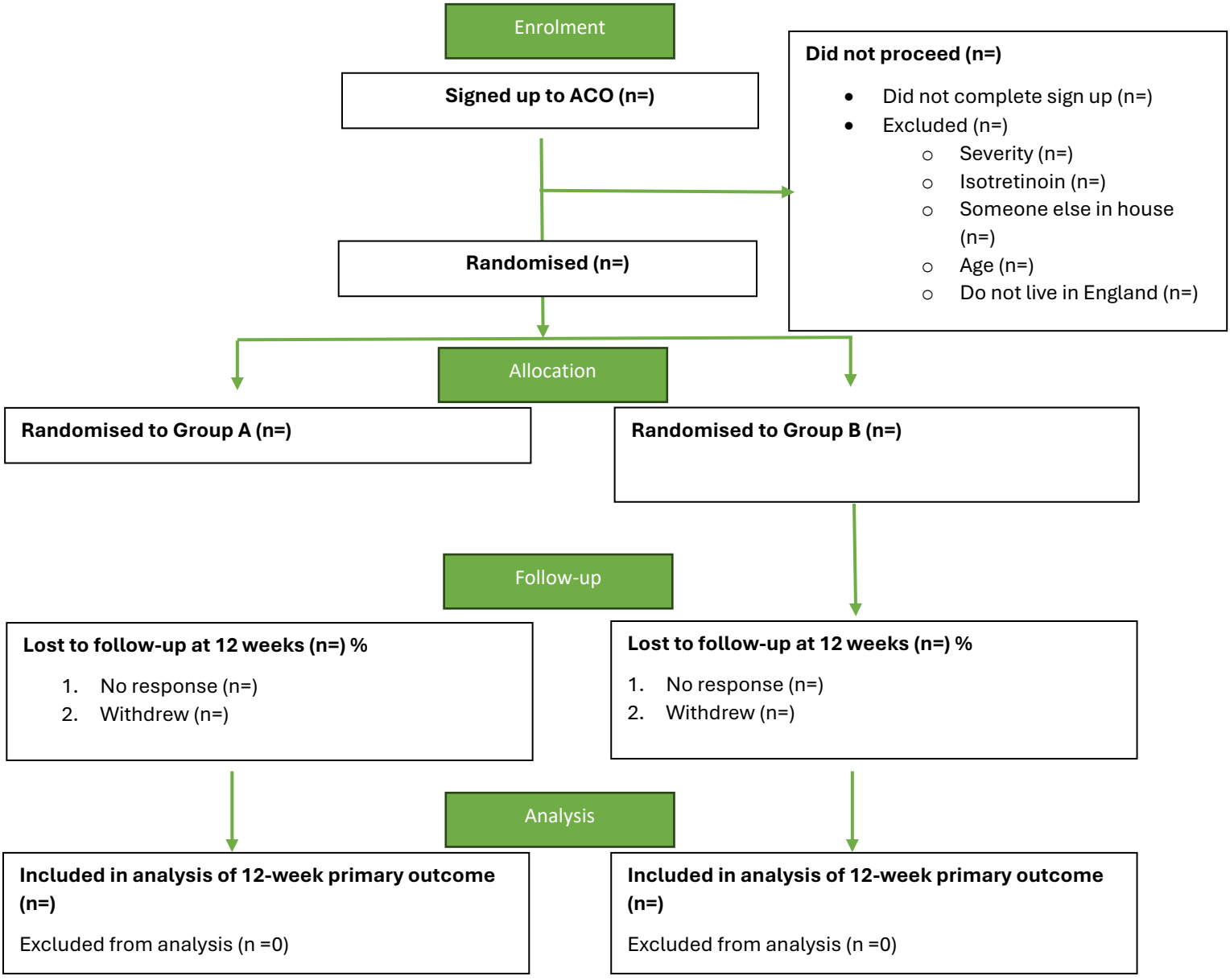
# 8. Other analyses

The cost-effectiveness evaluation of the intervention as specified in the protocol will be led by Professor Tracey Sach and will be specified in a separate Health Economics analysis plan. The team will also develop a separate analysis plan for the process evaluation, led by Professor Ingrid Muller.

## Table 1. Schedule of observations.

| Outcomes collected | Baseline | 12 weeks | 24 weeks | 36 weeks | 52 Weeks (end of study) |
|---|---|---|---|---|---|
| Screening questions (see protocol) | (pre) x | | | | |
| Demographics | x | | | | |
| Age of onset and duration of acne | x | | | | |
| Acne-QoL | x | x | x | x | x |
| Current use of topical acne treatments (which one) | x | x | x | x | x |
| Past use of topical acne treatments (which one) | x | | | | |
| Problematic Experiences of Therapy Scale (PETS) | x | x | | | x |
| Adherence to topical acne treatments (frequency of application) | x | x | x | x | x |
| Current use of oral acne treatments (which one) | x | x | x | x | x |
| Past use of oral acne treatments (which one) | x | | | | |
| Other treatments | x | x | x | x | x |
| Patient Enablement Instrument (PEI) | x | x | | | x |
| Prior belief about effectiveness of intervention | x | | | | |
| Use of online resources | x | x | | | x |
| Resource use | x | x | x | x | x |
| Patient Health Questionnaire (PHQ–4) | x | x | | | x |
| Brief Illness Perceptions Questionnaire | x | x | | | x |
| EQ-5D-5L | x | x | x | x | x |
| Short Warwick Edinburgh Mental Well-being Scale (SWEMWBS) | x | x | x | x | x |

## Figure 1 Consort Diagram



# References


1. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. Journal of Investigative Dermatology. 2014;134(6):1527–34.
2. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. The Lancet. 2012;379(9813):361–72.
3. Lown M, McKeown S, Stuart B, Francis NA, Santer M, Lewith G, et al. Prescribing of Long-term Antibiotic to Adolescents in Primary Care: a Retrospective Cohort Study. Society of Academic Primary Care Annual Scientific Meeting2020.
4. Walsh TR, Efthimiou J, Dréno B. Systematic review of antibiotic resistance in acne: an increasing topical and oral threat. The Lancet Infectious Diseases. 2016;16(3):e23–e33.
5. Purdy S, Langston J, Tait L. Presentation and management of acne in primary care: a retrospective cohort study. British Journal of General Practice. 2003;53:5.
6. Ip A, Muller I, Geraghty A, McNiven A, Little P, Santer M. Young people's perceptions of acne and acne treatments: secondary analysis of qualitative interview data. British Journal of Dermatology. 2020;183(2):349–56.
7. McLeod L, D., Fehnel S, E. , Brandman J, Symonds T. Evaluating Minimal Clinically Important Differences for the Acne-Specific Quality of Life Questionnaire. Pharmacoeconomics. 2003;21(15):1069–79.
8. Fehnel SE, McLeod LD, Brandman J, Arbit DI, McLaughlin-Miley CJ, Coombs JH, et al. Responsiveness of the Acne-Specific Quality of Life Questionnaire (Acne-QoL) to treatment for acne vulgaris in placebo-controlled clinical trials. Quality of Life Research. 2002;11(8):809–16.
9. Kirby S, Donovan-Hall M, Yardley L. Measuring barriers to adherence: validation of the problematic experiences of therapy scale. Disability and rehabilitation. 2014;36(22):1924–9.
10. Howie J, Heaney DJ, Maxwell M, Walker JJ. A comparison of a patient enablement instrument (PEI) against two established satisfaction scales as an outcome measure of primary care consultations. Family practice. 1998;15(2):165–71.
11. Broadbent E, Petrie KJ, Main J, Weinman J. The Brief Illness Perception Questionnaire. Journal of Psychosomatic Research. 2006;60(6):631–7.
12. Löwe B, Wahl I, Rose M, Spitzer C, Glaesmer H, Wingenfeld K, et al. A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. Journal of affective disorders. 2010;122(1-2):86–95.
13. Yiu HHE, Buckell J, Petrou S, Stewart-Brown S, Madan J. Derivation of a UK preference-based value set for the Short Warwick-Edinburgh Mental Well-being Scale (SWEMWBS) to allow estimation of Mental Well-being Adjusted Life Years (MWALYs). Social Science & Medicine. 2023;327:115928.