Statistical Analysis Plan

PSITRAIN: cluster-randomised trial of mental-health training and patient psychoeducation in Portuguese primary care (ISRCTN16612927)

Version 2.0 (draft) — Salvage analysis of the PSITRAIN trial

Trial registration: ISRCTN16612927 | Funder: Fundação para a Ciência e Tecnologia (PIC/IC/82737/2007)

Original trial period: 2011–2013 | This SAP: April 2026

This document specifies the statistical analyses that will be conducted on the recovered PSITRAIN dataset. It is finalised before the analytical team computes any inferential statistics on the recovered file. The trial was conducted between 2011 and 2013; this SAP is therefore pre-specified relative to the current re-analysis but not relative to the original trial conduct. A partial prior analysis (Neves 2023) of the WHO-5 outcome has been published as a Master's dissertation and is disclosed in §2.5; the analyses specified below for that single outcome cannot be considered fully blind. For all other outcomes, the analyses below are pre-specified.

1. Administrative information

Trial title (full)	Improving symptoms of patients affected by common mental health disorders in primary care: a cluster randomised controlled trial of a combined intervention.
Trial acronym	PSITRAIN
Trial registration	ISRCTN16612927
Sponsor	Instituto de Saúde Pública da Universidade do Porto (ISPUP); previously NOVA Medical School, Lisbon (NMS)
Funder	Fundação para a Ciência e Tecnologia (FCT), grant PIC/IC/82737/2007
Original protocol	FCT submission, 2007; ethics approval CEFCM-UNL 28/07/2011
Trial conduct	Recruitment 2011-08 to 2012-03; intervention 2012; follow-up to 2013-05
SAP version	2.0 — draft, April 2026
SAP timing	Pre-specified for the salvage re-analysis. Drafted before any inferential analysis on the recovered dataset by the analytical team. Disclosure of the prior partial Neves (2023) analysis in §2.5.

2. Background and trial design

2.1. Trial design

PSITRAIN is a parallel two-arm cluster-randomised controlled trial. The unit of randomisation is the Health Family Unit (HFU; Unidade de Saúde Familiar — primary care practice). Patients are nested within general practitioners (GPs), and GPs within HFUs. Allocation was 3 HFUs to the case arm and 2 HFUs to the control arm, balanced on GP count to ensure ≥14 GPs per arm.

2.2. Interventions

Case arm: an 8-hour skills-based mental health training programme for GPs (covering recognition, diagnosis, treatment, referral and general management of common mental disorders), plus a parallel 8-hour training for nurses and clinical psychologists who delivered a six-session weekly group psychoeducation programme of 75 minutes per session for patients with common mental disorders (CMD).

Control arm: a 2-hour mental-health awareness session for GPs and treatment as usual (TAU) for patients.

2.3. Eligibility

Patient-level eligibility (from the registered protocol): adults ≥18 years presenting consecutively to participating HFUs with at least one of (i) WHO-5 Wellbeing Index ≤ 7, (ii) CGI-S ≥ 4, or (iii) an ICPC-2 mental-health diagnosis. Exclusion criteria: chronic alcohol or drug abuse (ICPC-2 P15, P16, P19), dementia (P70), organic psychosis (P71), schizophrenia (P72), affective psychosis (P73), mental retardation (P85), eating disorders (P86), serious suicidal risk or history of mania, fewer than four years of schooling or inability to read Portuguese, age <18, or psychiatric consultation/admission in the prior three months.

2.4. Hypotheses

Primary hypothesis (from the registered protocol): patients in HFUs allocated to the combined training-plus-psychoeducation intervention will show greater improvement in depressive symptoms at 12 months than patients in HFUs receiving treatment as usual. Operationally: a lower mean BDI-II total score at the 12-month endpoint in the case arm compared to the control arm, after accounting for baseline BDI-II and clustering by HFU.

Secondary hypotheses: case-arm patients will show greater improvement at 12 months on anxiety (BAI), somatic symptoms (PHQ-15), wellbeing (WHO-5), and clinician-rated severity (CGI-S researcher) than control-arm patients.

Pre-specified hypothesis on suicidality: based on the mechanism of action of the combined intervention — improved GP recognition of common mental disorders, increased patient help-seeking through psychoeducation, and reduced stigma — we hypothesise that the case arm will show a greater reduction in suicidal ideation (BSI) at 12 months than the control arm. This hypothesis was a stated aim of the project at the design phase: the trial was disseminated under the title "Suicide prevention and improved management of common mental disorders" at the European Symposium on Suicide and Suicidal Behaviour (Sweden, 2012) and at a subsequent conference in Barcelona (2014). The hypothesis is further grounded in evidence from comparable European multi-level interventions, including the European Alliance Against Depression community programme (Hegerl et al. 2008, 2009, 2019).

2.5. Prior analyses on this dataset and the scope of the present SAP

A partial prior analysis of this trial has been published as a Master's dissertation: Neves ÂEMR (2023), Improving mental health care literacy in primary care: a controlled intervention study, Faculdade de Medicina da Universidade do Porto. Available at: https://repositorio-aberto.up.pt/handle/10216/152707.

The thesis analysed the WHO-5 wellbeing score at the 12-month endpoint as the primary outcome, on the full registered N = 348 sample. The analysis used a linear mixed-effects model with HFU as random intercept; missing-data handling combined Full Information Maximum Likelihood for the control arm and Multiple Imputation by Chained Equations for the intervention arm, applied separately on the basis of arm-stratified Little's MCAR test results. The thesis reported a significant time-by-treatment interaction favouring the intervention arm. The thesis did not analyse the registered primary outcome (BDI-II) as an outcome variable, nor did it report inferential between-arm analyses of BAI, PHQ-15, BSI, or CGI-S.

The present SAP goes beyond the thesis by: (a) aligning the primary analysis with the registered primary outcome (BDI-II at 12 months); (b) reporting all secondary outcomes specified at registration; (c) applying methods that the thesis did not, including HFU and GP nested random effects, a five-layer sensitivity hierarchy with multiple imputation under MAR and tipping-point analysis under MNAR, a modified-ITT framework that addresses the 6-case archival data loss honestly, and pre-specified subgroup analyses; and (d) elevating BSI (suicidality) to a pre-specified hypothesis with a two-part model handling zero-inflation (§6.1).

The analytical team is not blind to the published WHO-5 result. For WHO-5 specifically, the analyses specified in this SAP cannot be considered fully blind preregistration; they are

framed as a methodologically more rigorous re-analysis of the previously published outcome. For BDI-II (primary), BAI, PHQ-15, BSI, and CGI-S, no inferential between-arm treatment-effect analysis has been previously performed, and the analyses below are pre-specified.

Two prior conference posters disseminated the protocol and intervention design — Gusmão R, Justo M, Teixeira A. (2012, Sweden); and the same authors at Barcelona (2014). Neither poster reports inferential analyses of trial outcome data, and they are mentioned here for completeness only.

3. Analysis of populations

3.1. Modified intention-to-treat (mITT) — primary population

The primary analysis population is a modified intention-to-treat (mITT) set defined as all participants randomised by virtue of HFU cluster allocation, recovered in the analysis dataset, and analysed in their originally allocated arm, regardless of attendance, exposure to intervention components, or completion of follow-up. The label "modified" is used because 6 of the 348 originally randomised participants (per the ISRCTN registry) could not be located in the recovered analysis dataset (see Section 11.1). The mITT population is therefore N = 342 (168 cases, 173 controls, 1 with indeterminate allocation).

3.2. Per-protocol — secondary population

The per-protocol population is defined as mITT participants who, in the case arm, were allocated to a GP who completed the 8-hour training and (where applicable) attended at least 4 of the 6 psychoeducation sessions. In the control arm: allocated to a GP who attended the 2-hour awareness session. This sample size will be reported, but per-protocol effect estimation is pre-specified as a secondary, supportive analysis only, given the well-known biases of per-protocol analyses in cluster-RCT contexts.

3.3. Strict-sample sensitivity (post-hoc with respect to original protocol)

A pre-defined sensitivity analysis will be conducted on the strict sample population (N = 314) consisting of mITT participants who additionally met at least one validated baseline instrument cut-off: BDI-II ≥ 18, BAI ≥ 8, PHQ-15 ≥ 10, or BSI ≥ 1. This criterion was applied during data management but was not pre-specified in the registered protocol; it is reported here as a post-hoc sensitivity analysis to address potential heterogeneity arising from inclusion of participants whose CMD caseness rests solely on the screening tools (WHO-5, CGI-S or ICPC-2) without instrument-level confirmation.

3.4. Population summary

Population	N	Definition	Use
mITT	342	All recovered randomised participants, in allocated arm	Primary
Strict-sample sensitivity	314	mITT + ≥1 baseline instrument cut-off positive	Post-hoc sensitivity
Per-protocol	TBD	mITT + adherence to allocated intervention	Supportive secondary
Originally registered	348	Per ISRCTN16612927 registry	Reported in CONSORT only

4. Outcomes

4.1. Primary outcome

BDI-II total score at the 12-month endpoint. The 12-month endpoint is operationalised as the most recent follow-up assessment available between months 7 and 12 post-baseline, with assessments at months 7–11 carried forward (LOCF) where the 12-month assessment was missing (see CONSORT diagram and Section 5.3). BDI-II total ranges from 0 to 63 with higher scores indicating more severe depressive symptoms.

4.2. Secondary outcomes (continuous)

All measured at the 12-month endpoint, with the same LOCF rule as the primary outcome:

- BAI total score (Beck Anxiety Inventory; 0–63)
- PHQ-15 total score (Patient Health Questionnaire — Somatic; 0–30)
- BSI total score (Beck Scale for Suicide Ideation; 0–38) — pre-specified suicidality outcome (§2.4); analysed using a two-part model (§6.1)
- WHO-5 total score (Five Wellbeing Index; 0–25, higher = better wellbeing) — see §2.5 regarding non-blind status of this outcome
- CGI-S researcher-rated severity (1–7)

4.3. Secondary outcomes (categorical / responder analyses)

For each continuous outcome above, a responder analysis using the established clinically-meaningful improvement threshold for that instrument: BDI-II reduction ≥ 5 points (or final score < 14, the established remission threshold); BAI reduction ≥ 5 points; PHQ-15 reduction ≥ 3 points; WHO-5 increase ≥ 10% of scale (≥ 2.5 points); CGI-S improvement of ≥ 1 category. ICPC-2 mental-health diagnosis remission status at 12 months will also be reported descriptively. For BSI, a binary "any suicidal ideation" responder analysis (BSI = 0 vs BSI > 0 at 12 months) will accompany the continuous two-part model in §6.1.

4.4. Outcomes not analysed (with rationale)

The 6-month (T1) timepoint is removed from outcome analysis and reported descriptively only. As documented in the CONSORT diagram, the systematic 6-month assessment was abandoned during the trial due to resource constraints; only 35 of 342 recovered participants (10.2%) were assessed in the 7–11 month window, and these values are used as LOCF carry-forwards for the 12-month endpoint rather than analysed as a separate timepoint.

Suicide and parasuicide events as a separate outcome (i.e., adverse-event-style records of attempts or completions) are not available in the recovered dataset; suicidality is analysed via BSI questionnaire scores as specified in §6.1.

5. Primary analysis

5.1. Statistical model

Linear mixed-effects model fitted to the mITT population, with BDI-II at the 12-month endpoint as the dependent variable.

Fixed effects:

- Treatment arm (case vs. control; reference = control)
- Baseline BDI-II total (mean-centred) — to improve precision (ANCOVA-style adjustment)
- Sex (Female vs. Male; reference = Female)
- Age (mean-centred, continuous)

Random effects:

- Random intercept for HFU (cluster) — accounts for cluster-level variance
- Random intercept for GP nested within HFU — accounts for provider-level variance

The treatment effect is the fixed-effect coefficient on the case-vs-control indicator. Reported quantities: estimate, 95% CI, and p-value (two-sided, $\alpha = 0.05$). The intracluster correlation coefficient (ICC) at HFU level will be reported.

5.2. Statistical software

R 4.x using the lme4 package for fitting and lmerTest for Satterthwaite-approximated degrees of freedom. Stata 18 will be used as a cross-validation reference using mixed (REML estimation, Kenward-Roger DDF). Both will produce the same point estimates; small differences in CI/SE are expected and the R/lme4 result will be reported as primary. Data management is conducted in R (or pandas/Python, equivalent).

5.3. Handling of LOCF in the primary outcome variable

The primary outcome variable bdi_t2_locf is constructed as: (a) the observed 12-month BDI-II if available, otherwise (b) the most recent observed value at 7–11 months if available, otherwise (c) missing. The mixed-effects model accommodates the resulting missingness in the outcome under the missing-at-random (MAR) assumption inherent to maximum-likelihood estimation in mixed models. No additional imputation is performed in the primary analysis.

The LOCF construction is acknowledged as a deviation from a strict 12-month-only outcome and is reported transparently in the Methods. Sensitivity analyses on the observed-only 12-month outcome (Section 7.2) will quantify the impact.

6. Secondary analyses

6.1. Continuous secondary outcomes

BAI, PHQ-15, WHO-5 and CGI-S will each be analysed using the same mixed-effects specification as the primary, adjusting for the corresponding baseline value of that outcome plus sex and age, with HFU and GP as nested random intercepts.

BSI two-part model (pre-specified for suicidality):

BSI is heavily right-skewed with a high proportion of structural zeros (participants with no suicidal ideation at all). A standard linear mixed model would mis-specify the distribution and underestimate uncertainty. We therefore pre-specify a two-part (hurdle) model:

Part 1 (hurdle): Mixed-effects logistic regression on the binary indicator "any suicidal ideation present at 12 months" (BSI > 0 vs BSI = 0). Fixed effects: treatment arm, baseline BSI binary, sex, age. Random intercept: HFU. Reports odds ratio (95% CI) and a between-arm risk difference computed by post-estimation marginal-effects, with 95% CI by parametric bootstrap (B = 2000).

Part 2 (intensity, conditional on hurdle): Linear mixed-effects model on log(BSI + 1) at 12 months, restricted to participants with baseline BSI > 0. Fixed effects: treatment arm, log(baseline BSI + 1), sex, age. Random intercept: HFU. Reports back-transformed ratio of geometric means (95% CI).

A combined marginal effect (mean BSI difference between arms, integrating over the hurdle and intensity parts) will be reported as the primary BSI summary, with 95% CI by parametric bootstrap. The two-part model is fitted in R using glmmTMB; sensitivity refits with brms (Bayesian) will be reported in supplementary materials.

6.2. Responder analyses

Binary responder outcomes (defined in §4.3) will be analysed using mixed-effects logistic regression with the same fixed-effect specification (treatment, baseline value of the corresponding instrument, sex, age) and HFU random intercept. GP nested random effect retained where convergence allows; otherwise dropped. Reported: odds ratio (95% CI), risk difference (95% CI) by post-estimation, p-value.

6.3. Pre-specified subgroup analyses

Subgroup analyses on the primary outcome will be performed by including a treatment-by-subgroup interaction term in the primary model. Subgroups:

- Sex (Female vs. Male)
- Age (≤50 vs. >50 years)
- Baseline BDI-II severity (<29 vs. ≥29 — moderate vs. severe)
- Recruitment method (consecutive patients vs. prior diagnosis)

- ICPC-2 diagnosis profile (depression-only vs. anxiety-only vs. mixed/somatoform)
- Baseline BSI > 0 (any suicidal ideation at baseline) — pre-specified given the suicidality hypothesis (§2.4)

Subgroup analyses are exploratory; significance threshold for interaction tests is $\alpha = 0.05$ with no multiplicity correction, and findings will be reported as hypothesis-generating only.

7. Sensitivity analyses

Pre-specified sensitivity analyses on the primary outcome (BDI-II at 12 months), reported in this hierarchy:

7.1. Multiple imputation under MAR (sensitivity 1)

Multiple imputation by chained equations (MICE) generating 50 imputed datasets, imputing missing 12-month BDI-II values using the imputation model: baseline BDI-II, baseline BAI, baseline PHQ-15, baseline WHO-5, baseline CGI-S, age, sex, treatment arm, HFU. The primary mixed-effects model will be fitted to each imputed dataset and pooled using Rubin's rules.

7.2. Observed-cases-only (sensitivity 2)

The primary mixed-effects model refitted to the subset with observed 12-month BDI-II (n=153 across both arms; case=67, control=86), excluding LOCF carry-forward cases. Quantifies the impact of the LOCF construction.

7.3. Strict-sample (sensitivity 3, post-hoc)

The primary mixed-effects model refitted to the strict-sample population (N = 314) defined in Section 3.3. Tests robustness to inclusion of participants whose CMD caseness rests on screening tools alone.

7.4. Tipping-point analysis under MNAR (sensitivity 4)

A pattern-mixture tipping-point analysis to assess robustness under missing-not-at-random (MNAR) assumptions. Missing 12-month outcome values in each arm will be imputed under MAR, then perturbed by adding a δ (delta) penalty to the case arm only. The δ that "tips" the primary treatment-effect p-value above 0.05 will be reported, allowing the reader to judge whether plausible departures from MAR could overturn the primary conclusion.

The tipping-point analysis is conducted separately for BDI-II and BSI. The MNAR concern is methodologically strongest for BSI: participants experiencing worsening suicidal ideation may be systematically less likely to attend follow-up, creating informative censoring that no amount of MAR-based imputation can fix. The BSI tipping-point is therefore reported as a primary robustness check on the suicidality finding.

7.5. Per-protocol (sensitivity 5)

The primary model refitted to the per-protocol population (Section 3.2). Reported with the explicit caveat that per-protocol effect estimates are biased in the presence of differential adherence between arms.

8. Missing data

8.1. Outcome data

Approximately 50% of participants are missing the primary outcome at the 12-month endpoint (case 53.8%, control 50.3%). The mixed-effects model handles this under the MAR assumption; multiple imputation under MAR (Section 7.1) is the primary sensitivity layer; tipping-point analysis under MNAR (Section 7.4) tests robustness to departures from MAR.

A baseline-only vs completer comparison will be reported in the supplementary materials, comparing observed 12-month completers to non-completers on baseline characteristics, to assess MAR plausibility.

8.2. Baseline covariate data

Missing baseline values for covariates (sex, age, baseline outcome) are imputed using a single mean or mode imputation in the primary analysis (since missingness on baseline covariates is < 1% in the recovered dataset). A sensitivity check using complete-case-only baseline covariates will confirm.

9. Descriptive analyses

Two descriptive tables will be produced:

Table 1 — Baseline characteristics by arm (mITT, N=342). Continuous variables: mean (SD), median (IQR). Categorical: n (%). No formal hypothesis tests on baseline imbalance reported (per CONSORT 2010).

Table 2 — Outcomes by arm at baseline and 12-month endpoint, with adjusted between-arm difference and 95% CI.

9.1. Variables for Table 1

Demographics: age, sex (Female/Male). Clinical: ICPC-2 mental health diagnoses (counts of P74, P75, P76 and combinations). Baseline severity: BDI-II, BAI, PHQ-15, BSI, WHO-5, CGI-S clinician, CGI-S researcher. Cluster: GP count per arm, patient count per HFU. Recruitment method: consecutive patient vs. prior diagnosis.

10. Statistical principles

Significance level: two-sided $\alpha = 0.05$ for the primary outcome.

Multiplicity: no formal correction. The primary outcome is BDI-II; secondary outcomes are reported with 95% CIs and labelled as secondary, with explicit caveat in the Results that significance on secondary outcomes is exploratory.

Confidence intervals: 95%, two-sided, for all effect estimates.

Effect-size reporting: estimates of between-arm difference are reported on the original BDI-II metric; standardised mean difference (Cohen's d) reported alongside for cross-trial comparability.

Cluster-level reporting: ICC at HFU level reported for the primary outcome.

11. Deviations from registered protocol

The following deviations from the registered ISRCTN16612927 protocol are documented for transparency:

11.1. Sample size: registered N=348; mITT N=342 (six participants not recoverable from archival files).

11.2. Primary outcome: registered protocol named both Hamilton Depression Rating Scale and SF-36 mental health components as primary outcomes. The current SAP uses BDI-II, consistent with the ISRCTN registry record (which lists BDI-II as primary).

11.3. 6-month timepoint: registered as a primary assessment timepoint; retired during the trial due to resource constraints. Earlier 7–11 month assessments retained as LOCF for the 12-month endpoint.

11.4. Statistical method: registered protocol specified t-tests, chi-squared and Cox regression. The current SAP specifies mixed-effects models, which are the modern standard for cluster-RCT analysis and properly account for clustering and missingness.

11.5. Strict-sample inclusion: an additional inclusion criterion (≥1 baseline instrument cut-off positive) was applied during data management; reported here as a post-hoc sensitivity analysis (Section 7.3).

11.6. Primary outcome shift between protocol dissemination and registry submission: two conference posters (Sweden 2012 and Barcelona 2014) identified CGI-S as the primary outcome, with BDI-II / BAI / PHQ-15 / BSI as secondary outcomes. The ISRCTN registry record submitted in 2023 names BDI-II as the primary outcome. The reason for and timing of the shift between 2014 and 2023 cannot be reconstructed from the available archival materials. The current SAP follows the 2023 registry record (BDI-II primary), which is the most recent date-stamped specification of trial outcomes.

11.7. Prior partial analysis (Neves 2023): a partial analysis of WHO-5 has been published as a Master's dissertation; the present SAP cannot claim full preregistration blindness for the WHO-5 outcome (see §2.5 for full disclosure).

12. Reporting

12.1. CONSORT compliance

The trial will be reported in compliance with the CONSORT 2010 Statement and the CONSORT 2012 cluster RCT extension (Campbell et al. 2012, BMJ). The CONSORT flow diagram is as documented in PSITRAIN_CONSORT_Cluster_v2.docx.

12.2. Tables and figures

Tables: Table 1 (baseline by arm), Table 2 (outcomes by arm). Supplementary tables: missing-data analyses, sensitivity analyses, subgroup analyses.

Figures: CONSORT flow diagram, forest plot of treatment effects across primary and secondary outcomes, response trajectory plot (BDI-II baseline → 12 months by arm).

12.3. Target journal

A high-target submission is planned. Tentative shortlist (to be confirmed): British Journal of General Practice (BJGP), Lancet Regional Health – Europe, BMC Medicine, JAMA Network Open, BJPsych Open. Final journal selection will be made after the analysis is run, based on effect size and methodological strength.

12.4. Data and code availability

The signed Statistical Analysis Plan, the anonymised analysis dataset (PSITRAIN_analysis_ready_v3.csv / .dta), the variable manifest, the analysis code, and the post-analysis CONSORT flow diagram and tables will be deposited as supplementary documents on the trial's ISRCTN registry record (ISRCTN16612927). The ISRCTN entry serves as the primary, time-stamped archive. The ISPUP institutional repository will hold a backup copy. Deposition is consistent with the individual participant data sharing plan registered at ISRCTN, which states that the dataset will be published as a supplement to the results publication, and is subject to ISPUP institutional review.

13. SAP change log

Version	Date	Changes
1.0	April 2026	Initial draft.
2.0	April 2026	Disclosure subsection §2.5 added (prior Neves 2023 thesis analysis on WHO-5; conference posters disclosed). Suicidality elevated to a pre-specified hypothesis (§2.4) anchored on 2012/2014 conference posters. BSI two-part model pre-specified (§6.1). MNAR concern for BSI flagged (§7.4). New deviation §11.6 declaring CGI-S → BDI-II primary outcome shift between protocol dissemination and registry submission. New deviation §11.7 declaring non-blind status for WHO-5. Author list and CRediT roles formalised in §14.

14. Authorship, contributions, and approvals

14.1. Author list

The eventual paper will be authored, in order:

#	Name	Position	CRediT roles
1	**Edgar Mesquita**	First author	Methodology, Software, Formal analysis, Validation, Visualization, Writing — original draft (Methods, Results), Writing — review & editing
2	**Ângelo Emanuel Martins Rodrigues Neves**	Second author	Investigation (prior partial analysis published as MSc thesis, Neves 2023), Writing — review & editing
3	**Ana Teixeira**	Middle author	Investigation (intervention delivery and data acquisition during 2011–2013 fieldwork), Writing — review & editing
4	**Virgínia da Conceição**	Middle author	Methodology (limited contribution), Writing — review & editing
5	**Ricardo Gusmão**	Senior author, corresponding author	Conceptualization, Funding acquisition, Investigation (trial conduct 2011–2013), Project administration, Resources, Supervision, Writing — original draft (Introduction, Discussion), Writing — review & editing

Edgar's first authorship reflects his leadership of the formal analysis and the writing of the Methods and Results sections. He is currently a PhD student under the supervision of the senior author (R. Gusmão); his PhD topic is the imputation of error in suicide registry data, which is methodologically aligned with the BSI two-part model and the MNAR tipping-point analysis specified in §6.1 and §7.4. The supervisor-student relationship is disclosed transparently here, as standard biomedical-authorship practice; the credibility of the analyses rests on the pre-specification of methods in this SAP, the deposition of the SAP at ISRCTN before analysis, and the optional external review in §14.3.

14.2. Acknowledgements (template)

The Acknowledgements section of the eventual paper will recognise: Mariline Justo, who contributed to the original protocol design and conference dissemination (2012 Sweden, 2014 Barcelona) but is not part of the present analysis team; the participating Health Family Units (FF-Mais, Santa Maria-Benedita, Pinhal do Rei – Pólo Pataias, Ramada, Parque) and their general practitioners, nurses, and clinical psychologists; the patients who participated in the trial; and the Ethics Committee of the Faculdade de Ciências Médicas, Universidade NOVA de Lisboa.

14.3. Approvals

This SAP requires approval before being locked and deposited at ISRCTN. Approving signatures:

Senior Author / Principal Investigator:

Assinado por: **RICARDO DUARTE MIRANDA DE GUSMÃO**
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CARTÃO DE CIDADÃO

Ricardo Gusmão _____ Date: _____

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Data: 2026-05-13 às 10:52:46

Edgar Mesquita _____ Date: _____

Optional external reviewer:

_____ _____ Date: _____

After all signatures are obtained, the signed SAP will be deposited as a supplementary document on the ISRCTN16612927 registry record. The ISRCTN deposition date is the canonical pre-specification date for this analysis. No inferential between-arm analyses on the BDI-II, BAI, PHQ-15, BSI or CGI-S outcomes will be conducted before that date.