STATISTICAL ANALYSIS PLAN

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OFFICIAL TITLE

Efficacy of the MOLI Technique and Virtual Reality Versus Conventional Venipuncture for Pain and Anxiety in Paediatric Patients: A Three-Arm Randomised Controlled Trial

BRIEF TITLE / ACRONYM

MOLIVeR Trial

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SPONSOR

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ETHICS APPROVAL

Research Ethics Committee for Medicinal Products of Cantabria (CEIm Cantabria), reference 2024.249

Status of this Document

This Statistical Analysis Plan (SAP) was written after completion of data collection, for the retrospective registration of the MOLIVeR trial on ClinicalTrials.gov. It describes the analyses actually performed and reported for the primary and secondary objectives. The analysis planned in Section 5.8 of the Study Protocol is summarised in Section 9, together with the choices of statistical tests made according to the observed distribution of the variables.

1. Introduction

The MOLIVeR trial is a single-centre, parallel-group, three-arm (1:1:1) open-label randomised controlled trial comparing the MOLI technique (pinwheel-guided breathing distraction), immersive virtual reality (VR) and the conventional technique (CT) during peripheral venous catheter (PVC) insertion in paediatric patients aged 4 to 12 years at Hospital Universitario Marqués de Valdecilla (Santander, Spain). Recruitment took place from 1 November 2024 to 31 August 2025 and 201 participants were randomised (67 per arm).

2. Objectives

2.1 Primary Objective

To compare the perception of pain and anxiety during PVC insertion among the MOLI technique, immersive VR and the CT.

2.2 Secondary Objectives

To compare family member satisfaction, PVC insertion success rate, nurse satisfaction and procedure duration among the three techniques.

3. Randomisation and Blinding

A randomisation list generated with Epidat 4.2 by an independent statistician, in permuted blocks of variable size (6 and 9), was concealed in sealed, opaque, serially numbered envelopes. Participants and intervention providers were not blinded; primary outcomes were recorded by an observer external to the procedure.

4. Sample Size

A total of 201 participants (67 per arm) was required to detect a difference of at least 1 point in pain intensity (Faces Pain Scale-Revised), assuming a standard deviation of 0.5 points, a two-sided α of 0.05, a β of 0.20 and an anticipated loss rate of 5 % (GRANMO calculator, version 7.11).

5. Outcome Variables

Variable	Instrument / definition	Type	Time point
Pain (primary)	Faces Pain Scale-Revised, 0-10	Ordinal	After venipuncture
Anxiety (primary)	Groningen Distress Scale, 1-5	Ordinal	After venipuncture
Heart rate	Pulse oximetry, bpm; change = post − pre	Continuous	Before and after
Insertion success	Patent PVC at first attempt	Binary	Procedure
Procedure duration	Minutes from skin disinfection to dressing	Continuous	During
Blood sampling	PVC allowing blood sample collection	Binary	Procedure
Satisfaction	Family member and nurse, 5-point Likert	Ordinal	After venipuncture
Adverse events	Free text, by type	Categorical	Procedure

Baseline covariates: age, sex, triage priority (III/IV/V), DIVA score (difficult access ≥ 4), puncture site, catheter gauge, nurse age and paediatric experience.

6. Analysis Population

Intention-to-treat (ITT): all randomised participants analysed in the arm to which they were allocated.

7. Statistical Methods

7.1 Descriptive Statistics

Quantitative variables are summarised as mean and standard deviation (SD) or, when normality is not met, as median and interquartile range (IQR). Normality is assessed with the Shapiro–Wilk test within each arm. Categorical variables are reported as absolute and relative frequencies. Baseline characteristics are presented by arm.

7.2 Primary Analysis

Normality of both primary outcomes was rejected in all three arms (Shapiro–Wilk, $p < 0.01$). Overall comparisons among the three arms were therefore performed with the Kruskal–Wallis test.

Pairwise post-hoc comparisons (CT vs MOLI, CT vs VR, MOLI vs VR) were performed with the Mann-Whitney U test with Bonferroni correction for three comparisons (significance threshold $p < 0.0167$).

7.3 Effect Sizes

Test	Effect size	Small	Moderate	Large
Kruskal–Wallis	Epsilon squared (ε^2)	≥ 0.01	≥ 0.08	≥ 0.26
Mann–Whitney U	$r = \lvert Z \rvert / \sqrt{N}$	≥ 0.10	≥ 0.30	≥ 0.50

7.4 Secondary Outcomes

- Continuous and ordinal outcomes (heart rate, procedure duration, satisfaction): Kruskal–Wallis test, with Bonferroni-corrected Mann–Whitney U pairwise comparisons where applicable.
- Binary outcomes (first-attempt success, blood sampling): χ^2 test, or Fisher's exact test when expected frequencies are < 5.
- Adverse events: descriptive analysis by arm and type.

7.5 Subgroup Analysis

A subgroup analysis by age (4-6, 7-9 and 10-12 years), planned from the outset (Study Protocol, Section 5.8), was performed for the two primary outcomes using the same non-parametric framework within each stratum.

7.6 Missing Data

Primary outcomes were recorded in the same encounter as randomisation. No imputation was performed; missing values are reported by arm and variable.

7.7 Significance Level

All tests are two-sided with $\alpha = 0.05$; for post-hoc pairwise comparisons the Bonferroni-adjusted threshold is $0.05/3 = 0.0167$.

7.8 Software

Analyses were performed with IBM SPSS Statistics version 26.

8. Reporting

Results are reported following the CONSORT statement for parallel-group randomised trials, including a participant flow diagram. Effect sizes are reported alongside p-values for all primary comparisons.

9. Planned Analysis and Test Selection

Section 5.8 of the Study Protocol planned the use of IBM SPSS Statistics 26; normality assessment with the Kolmogorov-Smirnov test; parametric tests (Student's t, ANOVA, Pearson's correlation) when assumptions were met and non-parametric tests (Wilcoxon, Mann-Whitney U, Kruskal-Wallis, Spearman's correlation, chi-square) otherwise; Levene's and Mauchly's tests; outlier exploration with sensitivity analyses; the intention-to-treat principle; two-sided tests at $\alpha = 0.05$; and a subgroup analysis by age for the primary outcomes.

The analytical framework was applied as follows, according to the observed distribution of the variables:

Aspect	Study Protocol	Analysis performed
Normality test	Kolmogorov-Smirnov	Shapiro-Wilk
Primary comparison	Parametric or non-parametric depending on assumptions	Non-parametric (Kruskal-Wallis), as normality was rejected
Multiple comparisons	Not specified (Mann-Whitney U listed among the non-parametric tests)	Mann-Whitney U with Bonferroni correction ($p < 0.0167$)
Effect sizes	Not specified	ε^2 and r
Categorical variables	Chi-square	Chi-square or Fisher's exact test
Subgroup analysis by age	Planned (4-6, 7-9, 10-12 years)	Performed as planned, with the non-parametric framework
Software	IBM SPSS 26	IBM SPSS 26

These differences do not modify the trial hypothesis, the primary or secondary outcomes, the eligibility criteria or the interventions.