# Title

Yunshen Bai yb2584

## Abstract

Contents

[Title 1](#_Toc163565297)

[Abstract 1](#_Toc163565298)

[1. Introduction 3](#_Toc163565299)

[2. Data Summary 3](#_Toc163565300)

[3. Methods 4](#_Toc163565301)

[4. Results 5](#_Toc163565302)

[4.1 categorical data analysis 5](#_Toc163565303)

## Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder that not only affects joints but also may involve various organs in the body. Understanding the effectiveness of different treatments is crucial to improving patient outcomes. This report aimed at comparing the efficacy of two treatment for rheumatoid arthritis over a six-month period. The treatments compared were a combination of Disease-Modifying Antirheumatic Drugs (DMARDs) with Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) versus NSAIDs alone.

In this report, we perform longitudinal analysis on the rheumatoid arthritis study. Longitudinal analysis is a statistical method used to analyze data collected from the same subjects repeatedly over a period. This type of analysis is particularly relevant in studies where we want to assess how outcomes change over time or understand the time-dependent effects of treatments or interventions.

## Data Summary

The primary measure of success in this study was the proportion of patients who achieved the American College of Rheumatology 20% improvement criteria (ACR20). This primary endpoint was supplemented by seven secondary endpoints, including physician assessment of disease activity (PHYASMT), patient assessment of disease activity (PATASMT), number of painful joints (PAINJT), number of swollen joints (SWELLJT), visual analog pain scale (VAPS), C-reactive protein (CRP), and health assessment questionnaire (HAQ). These components are integral to a comprehensive evaluation of treatment impact, where a lower score typically indicates an improvement in condition.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **ACR20** | |  |  |
| **Treatment** | **1** | **0** | **Total** | **Proportion (%)** |
| 1 | 24 | 64 | 88 | 27.27 |
| 2 | 45 | 48 | 93 | 48.39 |
| **Total** | 69 | 112 | 181 | 38.12 |

Table 1. Distribution of ACR20 and Proportions by Treatment

The study involves two treatment groups: one receiving DMARD+NSAID (treatment 2) and the other receiving NSAID alone (treatment 1). A total of 181 patients participated in the study, with 88 receiving treatment 1 and 93 receiving treatment 2. The analysis of the ACR20 response shows a higher proportion of responders in the treatment group receiving treatment 2 compared to the group receiving treatment 1.

The dataset exhibits instances of missing data, specifically in C-reactive protein and health assessment questionnaire. Handling missing data is a critical aspect of statistical analysis and can be approached through various methodologies. In this report, we use LOCF to handle missing data. Last Observation Carried Forward (LOCF) is a method used in longitudinal data analysis to handle missing data, particularly in clinical trials. It involves substituting missing values for a participant with the most recent non-missing value available for that participant. While it's a simple and commonly used method, it's important to be aware that LOCF can introduce bias and should be applied with caution.

## Methods

In this report, endpoints will be analyzed including using method for categorical data analysis. We use CMH test to assess the association between two treatments. The Cochran-Mantel-Haenszel (CMH) test is a statistical analysis method used primarily in epidemiological studies to evaluate the association between an exposure and an outcome, while controlling for one or more confounding variables. It provides a way to test for an overall association between the exposure and the outcome across all strata. We will also perform an exploratory analysis using ACR20 with adjustment of center.

Analysis of Covariance (ANCOVA) will be employed to dissect the influence of treatment, center, and baseline measurements on the endpoints in this report. ANCOVA is a blend of analysis of variance (ANOVA) and regression that is used in statistical analysis. It allows you to compare one or more means while statistically controlling for variation associated with one or more covariate variables that can influence the dependent variable. ANCOVA assumes that the residuals are normally distributed and that the variances are equal across groups and homogeneity of regression slopes. The form of ANCOVA can be expressed as

Where is the overall mean, is the ith treatment effect, is the jth center effect, is the corresponding baseline and is the residual.

In this report, we will compare time to discontinuation for lack of efficacy using time-to-event analysis. Time-to-event analysis is a set of statistical methods used to analyze the expected duration of time until one or more events of interest occur. This type of analysis is particularly useful when subjects in a study are followed over time and the outcomes are not only whether an event occurred, but also when it occurred. The outcome of interest in this project is discontinuation for lack of efficacy. We use log-rank test to compare time to discontinuation for lack of efficacy of two treatments. The Log-Rank test is a non-parametric statistical test that is widely used in time-to-event analysis or survival analysis. The test is used to compare survival distributions of two or more independent groups.

## Results

### 4.1 Categorical Data Analysis

In this report, we use CMH test to assess the association between two treatments. The hypotheses for this test are

* Null hypothesis (): There is no association between treatments and proportion of ACR20 responders
* Alternative Hypothesis (): There is an association between treatments and proportion of ACR20 responders

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Test Group** |  | **DF** | **Pr>** | **OR** |
| Treatment 1 vs Treatment 2 | 8.4982 | 1 | 0.0036 | 2.5000 |

Table 2. Result of CMH test on the association between two treatments and proportion of ACR20 responders

The p-value of 0.0036 is less than the significance level of 0.05, leading us to reject the null hypothesis. This suggests that there is a statistically significant association between the two treatments with respect to the proportion of ACR20 responders. The Odds Ratio (OR) of 2.500 indicates that the odds of being an ACR20 responder is 2.5 times higher in Treatment 2 compared to Treatment 1.

However, medical conditions in different centers may affect the effectiveness of treatment. Therefore, we will perform an CMH test with adjustment of center. The hypotheses for this test are

* Null hypothesis (): There is no association between treatments and proportion of ACR20 responders across the centers
* Alternative Hypothesis (): There is an association between treatments and proportion of ACR20 responders across the centers

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Test Group** |  | **DF** | **Pr>** | **OR** |
| Treatment 1 vs Treatment 2  (controlling for centers) | 8.2713 | 1 | 0.0040 | 2.5009 |

Table 3. Result of CMH test on the association between two treatments and proportion of ACR20 responders across the centers

The p-value of 0.0040 is less than the significance level of 0.05, leading us to reject the null hypothesis. This indicates that significant associations between treatment and the proportion of ACR20 responders when controlling for the center. The odds ratio of 2.5009 implies that the odds of being an ACR20 responder are 2.5009 times higher in treatment 2 compared to the treatment 1.

### 4.2 ANCOVA

For these seven endpoints used to compute ACR20 response, we analyze them using ANCOVA – treatment, center, and baseline as covariates.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Endpoint** | **SV** | **DF** | **SS** | **MS** | **F value** | **p value** |
| **PHYASMT** | **Treatment** | 1 | 7.252 | 7.252 | 11.4259 | 0.0008 |
| **Center** | 26 | 27.278 | 1.049 | 1.6531 | 0.0312 |
| **Baseline** | 1 | 39.688 | 39.688 | 62.5342 | <0.0001 |
| **Residuals** | 174 | 110.432 | 0.635 |  |  |
| **PATASMT** | **Treatment** | 1 | 1.986 | 1.986 | 2.4958 | 0.1160 |
| **Center** | 26 | 32.130 | 1.236 | 1.5526 | 0.0517 |
| **Baseline** | 1 | 44.805 | 44.805 | 56.2935 | <0.0001 |
| **Residuals** | 174 | 138.488 | 0.796 |  |  |
| **PAINJT** | **Treatment** | 1 | 289.3 | 289.33 | 1.8191 | 0.1792 |
| **Center** | 26 | 14202.9 | 546.27 | 3.4346 | <0.0001 |
| **Baseline** | 1 | 2431.8 | 2431.82 | 15.2897 | 0.0001 |
| **Residuals** | 174 | 27674.6 | 159.05 |  |  |
| **SWELLJT** | **Treatment** | 1 | 875.4 | 875.44 | 10.9970 | 0.0011 |
| **Center** | 26 | 17926.8 | 8.6612 | 8.6612 | <0.0001 |
| **Baseline** | 1 | 2778.97 | 2778.97 | 34.9085 | <0.0001 |
| **Residuals** | 174 | 13851.6 | 79.61 |  |  |
| **VAPS** | **Treatment** | 1 | 243.4 | 243.4 | 4.0014 | 0.0467 |
| **Center** | 26 | 3566.0 | 137.15 | 2.2607 | 0.0010 |
| **Baseline** | 1 | 1766.1 | 1766.1 | 29.1100 | <0.0001 |
| **Residuals** | 174 | 10556.5 | 60.67 |  |  |
| **CRP** | **Treatment** | 1 | 31.20 | 31.20 | 12.3079 | 0.0005 |
| **Center** | 26 | 88.50 | 3.404 | 1.3426 | 0.1364 |
| **Baseline** | 1 | 264.55 | 264.55 | 104.3461 | <0.0001 |
| **Residuals** | 174 | 441.14 | 2.535 |  |  |
| **HAQ** | **Treatment** | 1 | 0.498 | 0.498 | 12.3079 | 0.0005 |
| **Center** | 26 | 15.420 | 0.5931 | 1.3426 | 0.1364 |
| **Baseline** | 1 | 0.061 | 0.061 | 104.3461 | <0.0001 |
| **Residuals** | 174 | 81.777 | 0.4699 |  |  |