

# Crow's Feet Severity Reduction Study

By  
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# Synopsis: Crow's Feet Severity Reduction Study

## Objective

The study aimed to evaluate the effectiveness of a specific intervention in reducing the severity of crow's feet among a diverse group of subjects over 28 days. It further sought to analyze the impact of demographic factors, including sex and race, on the extent of reduction, aiming to identify potential variations in treatment efficacy across different demographic groups.

## Methodology

The study is about 32 participants, with an equal representation of sexes and a mix of racial backgrounds to ensure a broad applicability of findings. Severity scores were measured at baseline (Day 0), midpoint (Day 14), and study conclusion (Day 28). They were assigned using a validated grading scale ranging from 0 (no wrinkles) to 9 (severe wrinkles). The cohort's demographic data, including sex and race, were also recorded. Statistical analyses, including descriptive statistics, Wilcoxon signed-rank tests, and percentage change calculations, were performed to assess changes in severity over time and across demographic subgroups.

## Statistical Analysis

The primary analysis was centered on the change in severity scores from baseline to Day 28, with the Wilcoxon signed-rank test evaluating the statistical significance of observed changes. A pre-defined alpha level of 0.05 was used to determine significance. Secondary analyses explored correlations between demographic factors and changes in severity scores.

## Key Findings

1. The study observed a gradual reduction in the mean severity scores of crow's feet from baseline to Day 28, suggesting the potential efficacy of the intervention.
2. The Wilcoxon signed-rank test confirmed a statistically significant decrease in crow's feet severity, with p-values significantly below 0.05.
3. Demographic analysis indicated variations in treatment response across different sex and racial groups, though these findings warrant further investigation to understand underlying factors.

## Conclusions

The study concluded that the specified intervention significantly reduced the severity of crow's feet over the study period. Demographic factors were found to contribute to variations in treatment outcomes, emphasizing the importance of personalized approaches in cosmetic dermatology. The findings suggest that further research is warranted to enhance the understanding of demographic influences on treatment efficacy and to refine intervention strategies for crow's feet reduction.

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# **1. Introduction**

## **1.1 Background on Crow's Feet Wrinkles**

Crow's feet, often referred to as laugh lines, are small wrinkles that emerge at the outer corners of the eyes. They are among the first signs of aging to appear on the face, primarily resulting from the loss of collagen and elasticity in the skin. Various factors contribute to the development and deepening of crow's feet, including but not limited to, repeated facial expressions (like smiling or squinting), sun exposure, smoking, and dehydration. These wrinkles can range from fine lines to more pronounced creases, depending on numerous individual factors, including genetics, skin type and lifestyle choices.

## **1.2 Significance of the Study**

The appearance of crow's feet can significantly affect an individual's self-perception and quality of life, leading to increased interest in cosmetic and therapeutic interventions aimed at mitigating these signs of aging. Despite the availability of various treatments ranging from topical creams to injectables and laser therapy, there remains a substantial demand for evidence-based assessments of their efficacy. This study responds to this demand by systematically evaluating the impact of a specified intervention over a 28-day period, contributing valuable insights to the field of cosmetic dermatology.

# **2. Study Objective**

The primary objective of this study is to assess the reduction in the severity of crow's feet among a cohort of subjects following a specified intervention over a 28-day period. Additionally, the study aims to explore the relationship between demographic factors (sex and race) and the extent of crow's feet reduction, seeking to identify any significant differences in treatment outcomes across various demographic groups. This objective is grounded in the hypothesis that the intervention will result in a measurable decrease in crow's feet severity, with potential variations in efficacy across different demographic profiles.

## **2.1 Rationale for the Study**

Understanding the effectiveness of interventions targeted at reducing crow's feet is crucial for advancing dermatological practice and offering patients evidence-based treatment options. Moreover, investigating the influence of demographic factors on treatment outcomes can provide insights into tailoring cosmetic interventions to meet the diverse needs of the population, enhancing patient satisfaction and treatment efficacy. This study aims to fill existing gaps in the literature by providing robust data on the short-term effects of a specific treatment on crow's feet, thereby aiding clinicians in making informed treatment recommendations.

# **3. Study Population**

## **3.1 Demographic Characteristics**

The study involved a diverse group of 32 participants, selected to represent a range of sexes, and racial backgrounds. This diversity ensures the study's findings are applicable to a wide demographic, reflecting the general population interested in treatments for crow's feet.

### 3.1.1 Sex Distribution

The study equally represented biological sexes, with 17 males (53.125%) and 15 females (46.875%) participating, to explore any sex-related differences in treatment efficacy.

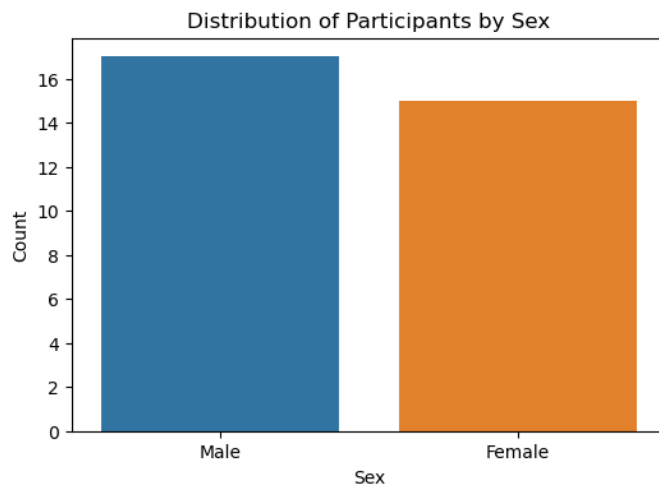


Fig 3.1.a Distribution of Participants by Sex

Percentage of Participants by Sex

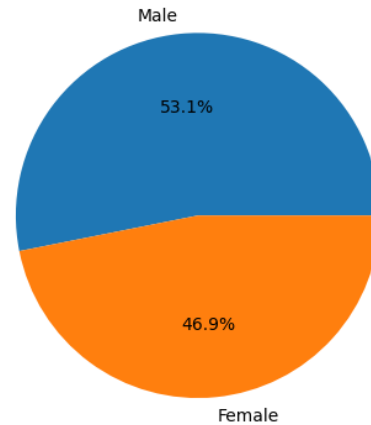


Fig 3.1.b Percentage of Participants by Sex

### 3.1.2 Racial Composition

Racial diversity was a key consideration, with the following breakdown: 12 Caucasian (37.5%), 12 Asian (37.5%), 4 Black (12.5%), and 4 identifying as Bi-racial (12.5%), to assess any potential racial variations in treatment response.

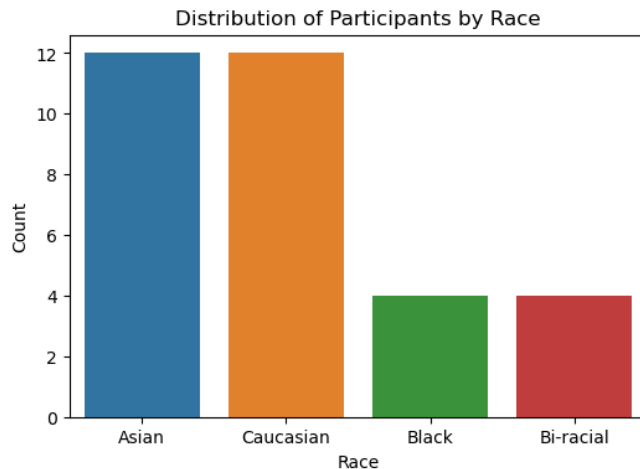


Fig 3.1.c Distribution of Participants by Race

Percentage of Participants by Race

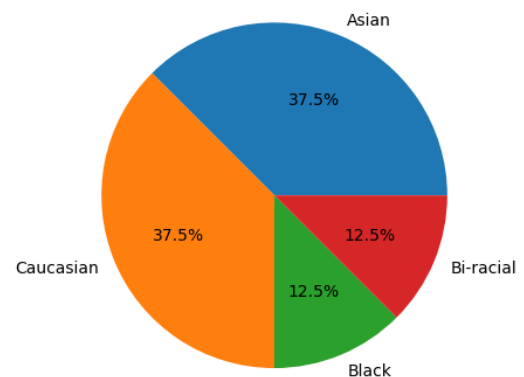


Fig 3.1.d Percentage of Participants by Race

The inclusion of various races and both biological sexes was pivotal in exploring any correlations between demographic factors and the extent of crow's feet reduction, shedding light on the treatment's universal applicability.

## 4. Efficacy Assessment

### 4.1 Baseline Characteristics

Crow's feet severity was quantitatively assessed using a validated numerical grading scale at three timepoints: baseline (Day 0), midpoint (Day 14), and study conclusion (Day 28). The scale ranged

from 0 (no wrinkles) to 9 (severe wrinkles), allowing for precise categorization of crow's feet severity.

**Initial Baseline Measurement (Day 0):** Participants' crow's feet were assessed and recorded to establish a baseline for comparison against future measurements. This initial assessment was crucial for observing the natural state of the crow's feet without any treatment effects.

**Midpoint Assessment (Day 14):** A follow-up assessment was conducted two weeks into the study to observe any early signs of change in the severity of the crow's feet. This would help in understanding the initial response to the treatment or intervention being assessed.

**Final Assessment (Day 28):** The last assessment was performed after 28 days to determine the final state of the crow's feet after the treatment period. This measurement was critical for assessing the efficacy of the intervention over a short-term period.

## 4.2 Statistical Analysis Plan

### 4.2.1 Primary Analysis

The primary endpoint was the change in crow's feet severity scores from baseline to Day 28. Statistical significance of the observed changes was evaluated using Wilcoxon signed-rank test with a pre-defined alpha level of 0.05.

### 4.2.2 Secondary Analysis

Exploratory analyses were conducted to assess changes in severity scores at the midpoint (Day 14) and to explore potential correlations between demographic factors (sex and race).

### 4.2.3 Criteria for Efficacy

A significant reduction in crow's feet severity was defined as a statistically significant decrease in the mean severity score from baseline to Day 28.

## 5. Results

### 5.1 Number of Cases per Timepoint

Throughout the study period, each participant was evaluated for the severity of crow's feet at three distinct timepoints. The assessments were conducted at baseline (Day 0), at a midpoint (Day 14), and at the conclusion of the study period (Day 28). The number of participants at each of these timepoints remained consistent, with no cases of dropout or missing data. This complete dataset ensures the integrity of the statistical analysis and supports the reliability of the study findings.

Time Point	Number of Participants
Day 0	32
Day 14	32
Day 28	32

Table 5.1.a Table summarizing the number of cases assessed at each timepoint.

### 5.2 Descriptive Statistics

Statistical Measure	Day 0	Day 14	Day 28
Mean	6.03	5.63	5.0

<b>Standard Deviation</b>	0.82	0.61	0.67
<b>Minimum</b>	5.0	5.0	4.0
<b>Median (50<sup>th</sup> Percentile)</b>	6.0	6.0	5.0
<b>Maximum</b>	8.0	7.0	6.0

Table 5.2.a Table showcasing the mean severity scores, along with measures of variability, at Day 0 (baseline), Day 14 (midpoint), and Day 28 (conclusion)

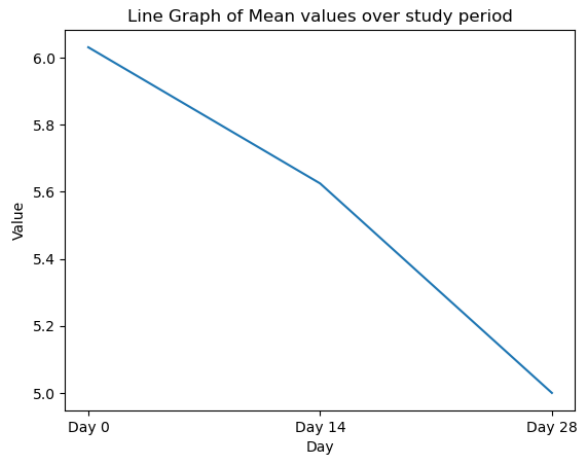


Fig 5.2.a Line graph of mean values of crow's feet over the study period

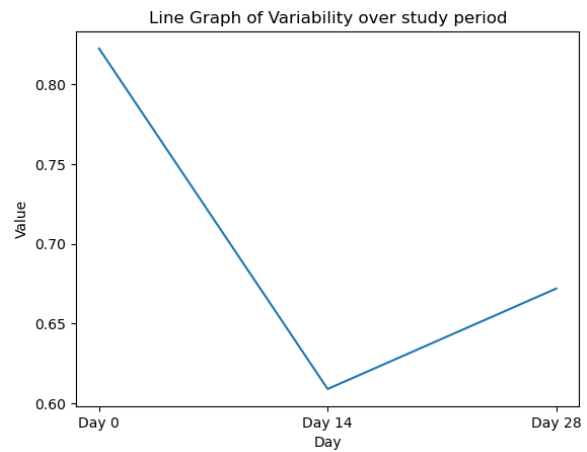


Fig 5.2.b Line graph of variability of crow's feet over the study period

1. A decreasing trend in mean severity scores from Day 0 to Day 28 suggests an overall improvement in the condition of crow's feet.
2. The standard deviation shows a decrease from Day 0 to Day 14 and a slight increase from Day 14 to Day 28, indicating changes in score dispersion over time.
3. Progressive decreases in minimum and maximum values across timepoints further support the trend of crow's feet severity reduction.

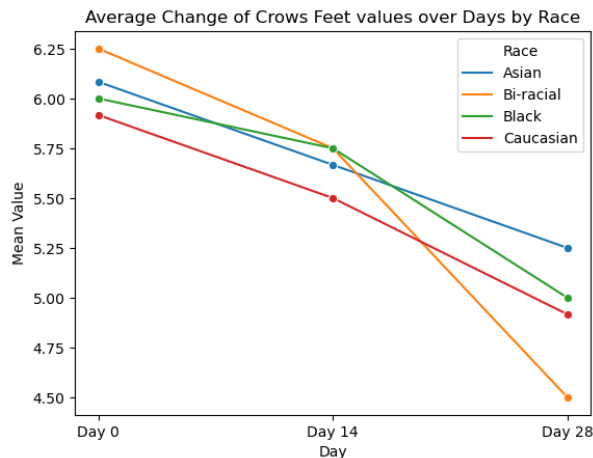


Fig 5.2.c Line graph of mean values of crow's feet over the study period differentiated by race

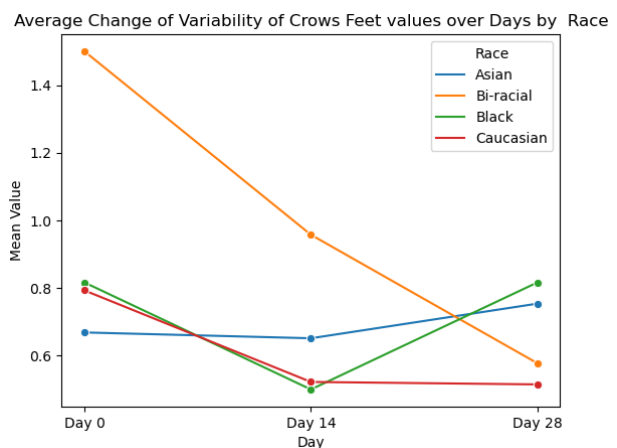


Fig 5.2.d Line graph of variability of crow's feet over the study period differentiated by race

### 5.2.1 Mean Severity Scores by Race

The analysis of mean severity scores by race indicates a reduction in crow's feet severity across all demographic groups from Day 0 to Day 28.

**Asian:** Starting with a mean severity score of 6.08 at baseline, there was a gradual decrease to 5.67 at Day 14, culminating in a mean score of 5.25 by Day 28.

**Bi-racial:** This group exhibited a mean severity score of 6.25 at baseline, which decreased to 5.75 at Day 14 and further to 4.50 by Day 28, showing the most considerable reduction among the groups.

**Black:** The participants started with a mean severity score of 6.00 and saw a reduction to 5.75 at Day 14, reaching 5.00 by Day 28.

**Caucasian:** The mean severity score reduced from 5.92 at baseline to 5.50 at Day 14, and down to 4.92 at Day 28.

These findings suggest a consistent treatment effect across all racial groups, with the Bi-racial group showing the most significant change over the study period.

### 5.2.2 Variability of Severity Scores by Race

The standard deviations (STDs) provide insight into the variability of the treatment response within each racial group.

**Asian:** The variability in severity scores slightly increased from baseline (STD: 0.67) to Day 28 (STD: 0.75).

**Bi-racial:** There was a notable decrease in variability from a high STD of 1.50 at baseline to 0.58 by Day 28, indicating a more uniform response to treatment over time.

**Black:** The variability remained consistent from baseline (STD: 0.82) to Day 28 (STD: 0.82), despite the reduction in mean severity scores.

**Caucasian:** The group's variability decreased slightly over the study period, from 0.79 at baseline to 0.51 by Day 28, suggesting a homogenous response to the treatment.

The reduction in standard deviation across most racial groups, along with the decrease in mean severity scores, indicates a positive response to the treatment with a trend towards less variability in outcomes by Day 28.

The descriptive statistics collectively indicate a positive trajectory towards reducing the severity of crow's feet throughout the study, providing an initial quantitative confirmation of the intervention's efficacy.

## 5.3 Percentage Change in Severity Scores

The effectiveness of the intervention over the 28-day period was quantitatively assessed by examining the percentage change in severity scores from the baseline at two subsequent timepoints. This analysis allows for an evaluation of the treatment's impact over time relative to the starting condition of each participant.



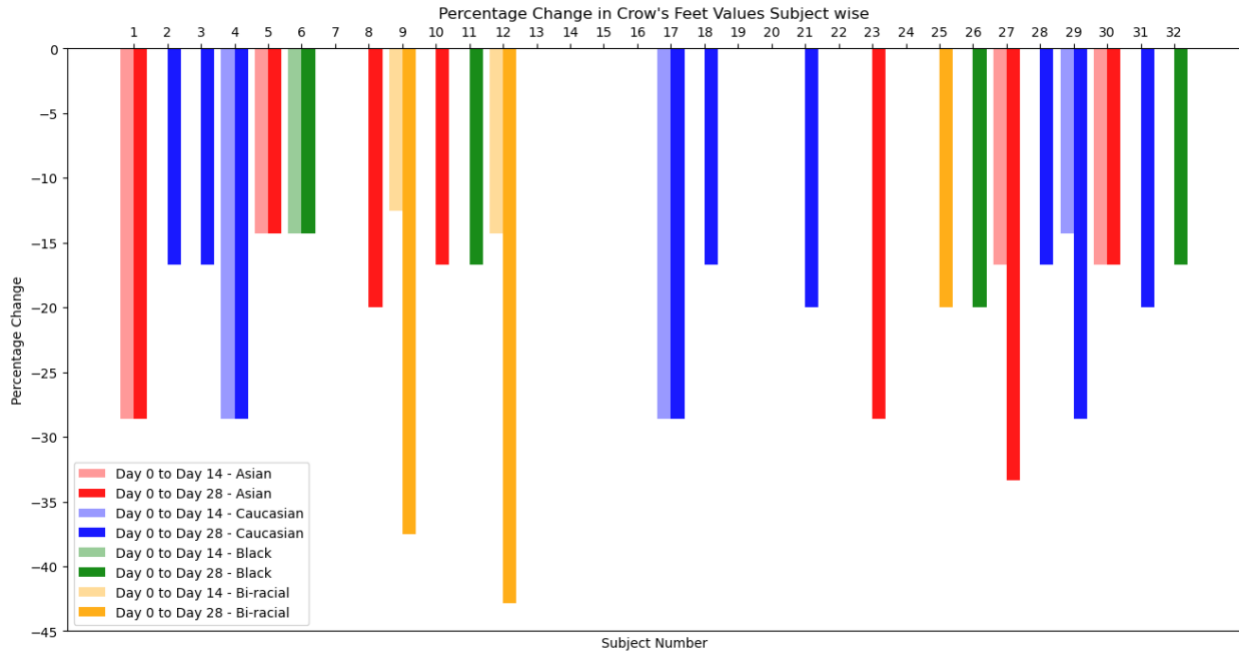


Fig 5.3.a Distribution of percentage change in crow's feet values

- The majority of participants experienced a reduction in crow's feet severity, pointing to the potential effectiveness of the intervention.
- The range of response highlights the need for individual assessment when considering treatment efficacy.

### 5.3.1 Race-wise analysis of percentage change

In the comprehensive analysis of treatment efficacy stratified by race and sex, distinct patterns in the percentage change of crow's feet severity scores were observed at Day 14 and Day 28, compared to baseline measurements.

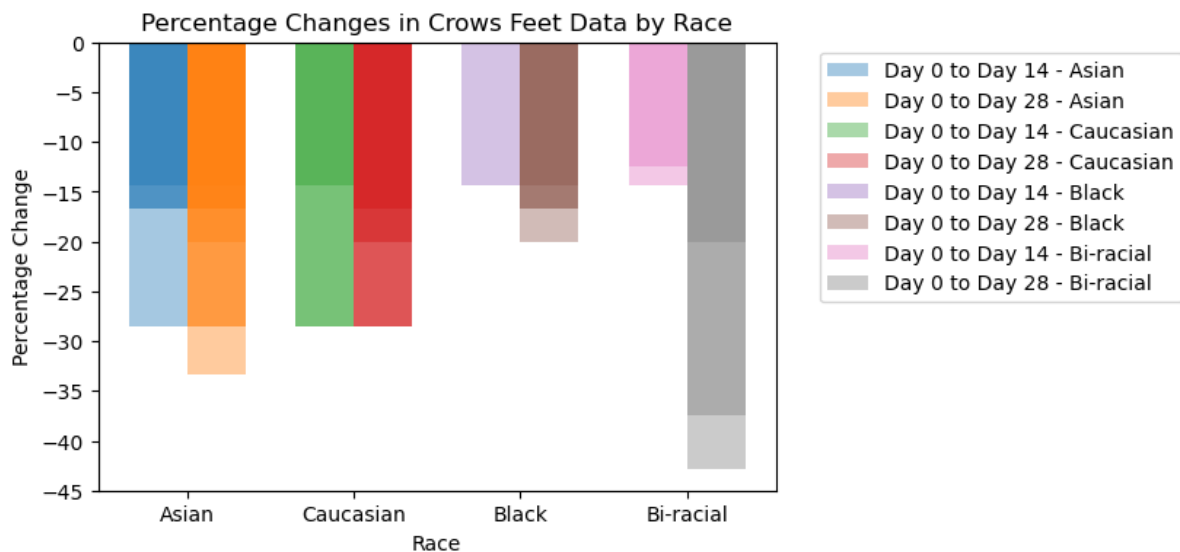


Fig 5.3.b Distribution of percentage change in crow's feet values by Race

### Asian Participants:

Among females, there was a range in response, with one individual showing no change at Day 14 but a 20% reduction by Day 28, indicating a delayed response to the treatment. Another showed consistent reductions at both timepoints, whereas one subject experienced an increase in the percentage reduction from Day 14 to Day 28, suggesting a progressive response.

Asian males exhibited a similar variation, with one participant showing a significant reduction at both Day 14 and Day 28, while others had either no change at Day 14 or a reduction by Day 28.

### Bi-racial Participants:

Female participants showed notable percentage decreases in severity. One individual had a significant reduction by Day 28, suggesting a potential delayed yet substantial response to the treatment.

### Black Participants:

Female participants showed both immediate and delayed treatment responses, with some showing no change at Day 14 but a reduction by Day 28. One male participant showed no change at Day 14, followed by a reduction at Day 28.

### Caucasian Participants:

Among females, one subject experienced a substantial reduction at both timepoints, whereas another had no initial change but a reduction at Day 28.

Caucasian males demonstrated diverse treatment responses, with some showing no change at Day 14 but improvements by Day 28, while others experienced a significant reduction at both timepoints.

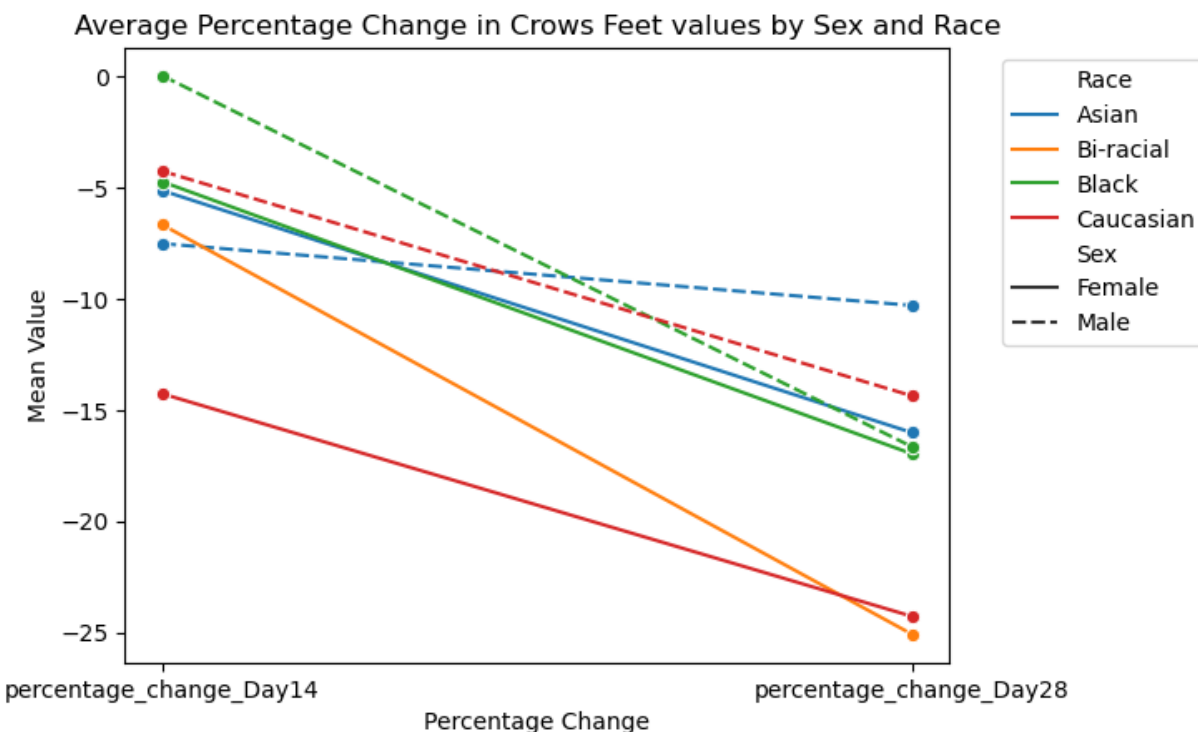


Fig 5.3.c Line graph showing percentage change in crow's feet values by Race and Sex of subjects.

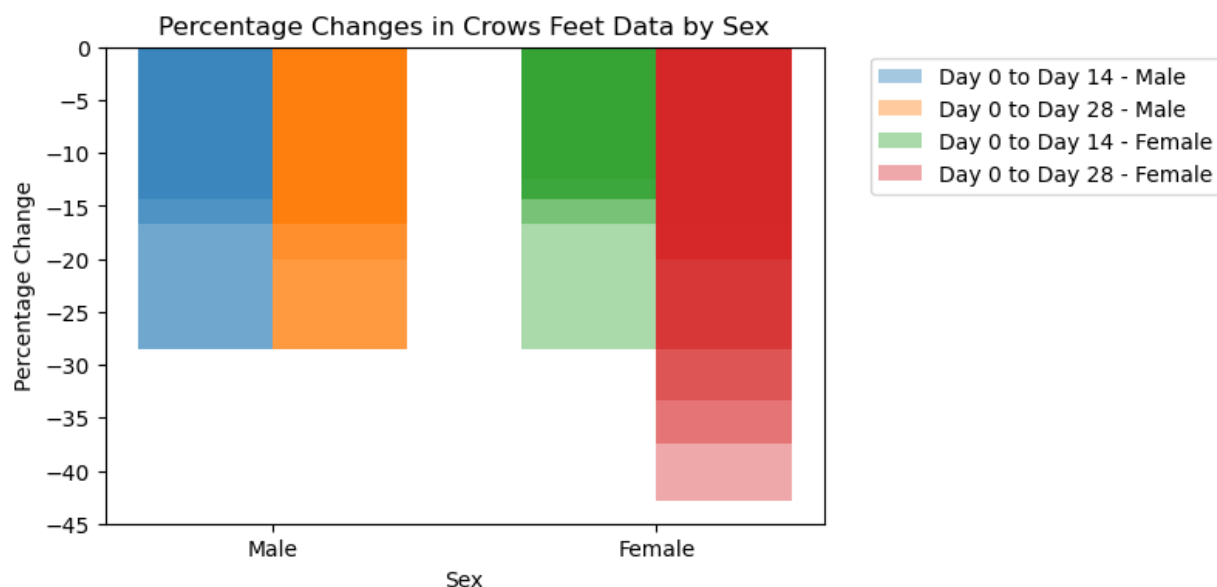


Fig 5.3.d Distribution showing percentage change in crow's feet values by Sex.

### 5.3.2 Race wise analysis of Non-Progressing Subjects

In the analysis of the study's outcomes, particular attention was given to the subgroups where participants exhibited no change in the severity of crow's feet over the 28-day period. This was characterized by consistent severity scores at the baseline (Day 0), midpoint (Day 14), and conclusion (Day 28) of the study.

#### Findings by Demographic Subgroups:

**Asian Females:** Two participants, identified as subject numbers 14 and 15, showed no variation in severity scores throughout the study period, remaining at severity levels of 5 and 6, respectively.

**Asian Males:** Three participants in this subgroup, subject numbers 7, 16, and 22, also demonstrated no change, maintaining a constant severity score of 6 across all timepoints.

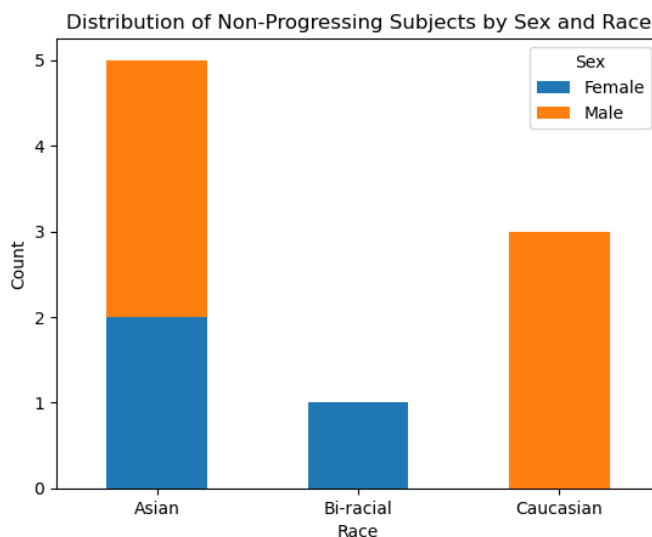


Fig 5.3.e Distribution showing non-progressive crow's feet values by Race and Sex.

**Bi-racial Females:** A single participant, subject number 13, exhibited no change in the severity score, which remained steady at 5.

**Caucasian Males:** In this demographic, subjects numbered 19, 20, and 24 displayed no progression or regression in severity scores, with subject 19 remaining at a score of 6, and subjects 20 and 24 consistently scoring 5.

### **Interpretation:**

The lack of change in severity scores across these participants suggests that the intervention employed in the study did not produce a measurable effect for them within the specified timeframe. This could be indicative of several possibilities, including but not limited to, the intervention's ineffectiveness for certain individuals, a plateau effect where the initial severity of crow's feet could not be improved with the given treatment, or the natural variability in the aging process that is resistant to the intervention used.

## **5.4 Wilcoxon Signed-Rank Test Results**

To assess the statistical significance of changes in crow's feet severity scores from Day 0 to Day 14 and Day 0 to Day 28 among 32 subjects, the Wilcoxon signed-rank test, a non-parametric statistical hypothesis test, was employed. This test is suitable for paired samples where the data does not necessarily follow a normal distribution. It evaluates whether the median of the paired differences is zero, which in the context of this study, would imply no median change in severity scores from baseline at the respective timepoints.

### **5.4.1 Hypotheses**

For both comparisons (Day 0 vs Day 14 and Day 0 vs Day 28), we formulated the following null and alternative hypotheses:

**Null Hypothesis (H0):** There is no median difference in crow's feet scores between the two time points being compared.

**Alternative Hypothesis (H1):** There is a median difference in crow's feet scores between the two time points being compared.

### **5.4.2 Methodological Choices**

To conduct the Wilcoxon signed-rank test, specific choices regarding the handling of zero differences and the application of the continuity correction were taken:

**Zero Method ('zsplit'):** The `zero_method='zsplit'` option is considered to evenly distribute zero differences among positive and negative ranks. This approach was selected because zero differences—cases where the treatment had no effect—are informative in our context. Splitting zero ranks allows for a more nuanced analysis that considers the possibility of no change as a distinct outcome.

**Continuity Correction (True):** Given the moderate sample size of our study, we applied the continuity correction (`correction=True`) to the test. This adjustment is made to account for the discrete nature of the Wilcoxon signed-rank test statistic when approximating a continuous distribution. It is a conservative approach that slightly increases the robustness of our p-value calculation, making our statistical inference more reliable.

## **Outcomes:**

**Day 0 vs Day 14:** The Wilcoxon signed-rank test yielded a statistic of 126.5 with a p-value of 0.007565899283536108, indicating a statistically significant median difference in crow's feet scores from Day 0 to Day 14.

**Day 0 vs Day 28:** For this comparison, the test produced a statistic of 22.5 with a p-value of 4.679742721290915e-06, also indicating a statistically significant median difference in crow's feet scores from Day 0 to Day 28.

## **Comparison to Non-Corrected Approach**

The choice to use the *zsplit* method and apply a continuity correction differs from not using these adjustments in that it provides a more conservative and nuanced analysis of our data. Without these adjustments, the test might underestimate the presence of zero differences (no change) and potentially overestimate the significance of our findings due to the discrete nature of the test statistic not being accounted for.

The results of the Wilcoxon signed-rank tests for both time comparisons clearly reject the null hypothesis, indicating significant reductions in crow's feet scores at both Day 14 and Day 28 compared to Day 0. This suggests that the treatment is effective in reducing crow's feet over the studied period. The methodological choices made, including the use of *zsplit* and the continuity correction, ensure that our analysis robustly accounts for the nuances in our paired sample data, providing a reliable basis for our conclusions.

# **6. Summary of Findings**

## **6.1 Efficacy of Intervention on Crow's Feet Reduction**

**Severity Score Reduction:** There was a significant decrease in the mean severity scores of crow's feet, from an initial average of 6.03 at baseline to 5.0 at the study's conclusion on Day 28. This reduction demonstrates the intervention's effectiveness in mitigating the appearance of crow's feet.

**Change Over Time:** The severity scores progressively declined from Day 0 through Day 28, with interim assessments at Day 14 indicating early signs of improvement. This trend underscores the treatment's continuous impact over the study period.

**Variability in Treatment Response:** The slight fluctuation in standard deviation from 0.82 at baseline to 0.67 at Day 28 suggests a general homogenization in participant responses to the treatment. This indicates that, while individual responses varied, there was a consistent trend towards improvement.

**Statistical Significance:** The application of the Wilcoxon signed-rank test revealed statistically significant reductions in crow's feet severity at both the midpoint and conclusion of the study compared to baseline (p-values of 0.0075 for Day 14 and approximately 4.67e-06 for Day 28), solidifying the intervention's efficacy.

## **6.2 Demographic Insights**

**Demographic Influence:** The study's balanced representation of sexes and diverse racial composition enabled an inclusive assessment of the intervention's efficacy across different demographic groups. This diversity ensures the findings' broader applicability and relevance to the general population seeking treatment for crow's feet.

**Race and Sex Analysis:** Examination of treatment outcomes by demographic subgroups revealed that all groups experienced a reduction in crow's feet severity, with variations in the extent of improvement. This highlights the intervention's universal benefit while also pointing to the potential for tailoring treatments based on demographic characteristics to optimize outcomes.

### 6.3 Overall Conclusions

**Treatment Effectiveness:** The intervention demonstrated a clear and statistically significant effectiveness in reducing the severity of crow's feet over the 28-day study period. This is evidenced by the overall decrease in mean severity scores, the progressive improvement observed at each assessment point, and the statistical analyses confirming these findings.

**Impact of Demographic Factors:** While the treatment was effective across all demographic groups, the variance in response suggests that factors such as sex and race may influence the extent of improvement. This underscores the importance of considering these factors in clinical practice to maximize treatment efficacy and patient satisfaction.

**Clinical Implications:** The significant and consistent reduction in crow's feet severity across a diverse participant group supports the intervention's potential as a valuable treatment option in cosmetic dermatology. These findings contribute important insights to the field, aiding clinicians in making informed recommendations and tailoring treatment approaches to meet individual patient needs.

## 7. References

- <https://www.mdpi.com/2077-0383/12/19/6326>
- [https://journals.lww.com/dermatologicsurgery/abstract/2021/04000/phase\\_i\\_iii\\_clinical\\_trial\\_to\\_evaluate\\_the\\_safety.17.aspx](https://journals.lww.com/dermatologicsurgery/abstract/2021/04000/phase_i_iii_clinical_trial_to_evaluate_the_safety.17.aspx)
- <https://classic.clinicaltrials.gov/ct2/show/NCT01951742>
- <https://ctv.veeva.com/study/clinical-trial-to-evaluate-ant-1401-in-crows-feet>
- <https://aesthetic-solutions.com/wp-content/uploads/2017/09/61CV-Efficacy-and-Safety-of-OnabotulinumtoxinA-for-the-Treatment-of-Crows-Foot-Lines.pdf>