**Project 0: Investigation on the effect of a new gel to gum disease**

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**Introduction:** Scientists want to know whether a new gel treatment is effective to gum disease. 130 participants were recruited through a single midwestern dental research clinic, and randomly assigned to 5 arms: (1) placebo group, (2) control group (no gel given), and three groups receiving gel with low (3), medium (4) and high (5) concentrations of the active ingredient respectively. Participants were asked to apply the gel on their gum twice a day. The subjects were assessed at baseline and one-year visit. Pocket depth and average attachment loss (measurements at 1 year with the subtraction of measurements at baseline) were measured at many different sites. Averaged measurements were recorded.

The following variables are in the dataset: patient id, treatment group, gender, age, race, smoker status, number of sites, average pocket depth at baseline and at one-year visit as well as average attachment loss at baseline and at one-year visit. The null hypothesis is that the new gel treatment does not have significant effect on change between post and pre-average pocket depth and attachment loss.

**Methods:**

Logistic regression was performed to check the association between the status of missing oral measurements at one-year visit and other predictors. Participants with missing oral measurements were excluded. Multinomial regression was performed to check the difference of sample sizes between five treatment groups with respect to demographic information and oral measurements. The significant level for this study is set as 0.05.Demographic statistics and measurement statistics for each treatment group were calculated. The race levels were combined as “White” vs. “Non-white” because race was not a character that we were really interested in and the sample sizes of people in other levels were very small.

Univariate regression: The change in average pocket depth and attachment loss were used as two outcomes. Other demographic variables and baseline measurements were used as predicters. For numeric predictors, the associations between outcomes and baseline measurements, sites as well as age were evaluated by simple linear regression. We did not categorize age to avoid losing pattern. For categorical variables, the assumption of homogeneity (equal variance between groups) was assessed by Levene's Test for gender, race, and smoke status by treatment group. One-way ANOVA were used on those variables who did not violate this assumption. The change in attachment loss between gender groups violated constant variance, therefore Welch's ANOVA was used.

Multivariate regression: Linear regression was used. Two sets of models were fitted. For the first set of models, change in attachment was the outcome. Treatment group was a predictor and attachment loss at baseline was a covariate. For the second set of models, change in pocket depth was the outcome. Treatment group was a predictor and average pocket depth at baseline was a covariate. Those two sets of models were adjusted for age, gender, race, smoke status, and sites. Backward selection was used. We did not use longitudinal model because we were not interested in whether the measurements at one year and at baseline were jointly associated with the treatment or not. In addition, we chose to use simpler model because it is easier to interpret. If the associations between treatment groups and change in measurement were significant, pairwise t-tests among the treatments would be carried out.

Diagnose: For those residual plots showed slightly heteroscedasticity, Lagrange multiplier tests and Q-statistics test were performed to test constant variance. We used Cook’s distance plot and studentized residual to diagnose influential points and outliers. After removing the outlier, the model was fitted again to check the difference.

Table 1 Characteristics by treatment group

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristics** | **Treatment group** ### | | | | | **Total number** | **P-value** |
| **Placebo(n=23)** | **Control(n=23)** | **Low(n=21)** | **Medium(n=20)** | **High(n=16)** |
| Demographics |  |  |  |  |  |  |  |
| Male (N) | 10(43.5%) | 7(30.4%) | 9(42.9%) | 7(35.0%) | 3(18.8%) | 36(35.0%) | 0.99 |
| White(N) | 21(91.3%) | 20(87.0%) | 17(81.0%) | 19(95.0%) | 14(87.5%) | 91(88.4%) | 0.34 |
| Age, Mean±sd | 47.2±8.86# | 51.4±10.16 | 51.5±10.26 | 48.6±9.87 | 52.6±10.71 | 50.2±9.95 | 0.47 |
| Smoker (N) | 10(43.5%) | 7(30.4%) | 6(28.6%) | 8(42.1%)## | 5(31.3%) | 36(35.3%) | 0.85 |
| Sites, Mean±sd | 159.7±10.66 | 153.9±11.24 | 161.7±8.16 | 153.5±17.12 | 158.3±8.73 | 157.4±11.89 | 0.25 |
| Attachment loss at baseline Mean±sd | 1.8±0.66 | 2.5±0.65 | 2.1±1.09 | 2.2±0.67 | 2.3±1.01 | 2.2±0.84 | 0.06 |
| Attachment loss after 1 year, Mean±sd | 1.7±0.54 | 2.3±0.55 | 2.1±1.06 | 2.2±0.65 | 2.1±0.92 | 2.1±0.77 | 0.13 |
| Change in attachment loss, Mean±sd | -0.1±0.24 | -0.2±0.28 | -0.02±0.27 | -0.01±0.23 | -0.2±0.33 | -0.1±0.28 | 0.07 |
| Pocket depth at baseline, Mean±sd | 3.1±0.39 | 3.3±0.49 | 3.2±0.64 | 3.0±0.42 | 3.2±0.28 | 3.2±0.47 | 0.38 |
| Pocket depth after 1 year, Mean±sd | 2.7±0.48 | 2.9±0.46 | 3.0±0.58 | 2.8±0.47 | 2.8±0.42 | 2.9±0.49 | 0.39 |
| Change in Pocket depth, Mean±sd | -0.3±0.28 | -0.3±0.23 | -0.2±0.28 | -0.2±0.27 | -0.4±0.24 | -0.3±0.27 | 0.11 |

# One subject with missing age; ## One subject with missing smoke status

###Unbalanced group size due to no re-visit

**Result:** The single midwestern dental research clinic enrolled 130 people. They were randomized into five groups with group size=26. One participant was with missing age and another was with missing smoke status. After excluding missing outcomes at one-year visit, 23 participants were in the placebo group, 23 participants were in the control group, 21 participants were in the low concentration group, 20 participants were in the medium concentration group, and 16 were in the high concentration group. Participants ranged from age 28 years to 74 years, with mean of 50 with 10 standard deviation. Most of participants were white (88.3%). Many of participants were women (65.1%). Many of participants are non-smokers (64.7%). Multinomial regression showed that the distributions of variables at baseline did not have association between treatment groups (Table 1).

Table 2 Change in attachment loss by treatment groups and covariates

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristics** | **Change in attachment loss** | | | | |
|  | P-value in univariate test | Regression coefficient in multivariate regression | P-value in multivariate regression | Regression coefficient after removing an outlier | P-value in multivariate regression after removing an outlier |
| Gender (Female as reference) | 0.070 | 0.04±0.055 | 0.52 | 0.04±0.052 | 0.44 |
| Race (Non-white as reference) | 0.97 | 0.10±0.082 | 0.24 | 0.07±0.079 | 0.35 |
| Age | 0.079 | -0.003±0.0027 | 0.24 | -0.003±0.0026 | 0.21 |
| Smoker (Non-smoker as reference) | 0.22 | 0.08±0.054 | 0.13 | 0.07±0.052 | 0.2 |
| Sites | 0.10 | -0.002±0.0026 | 0.52 | -0.0007±0.0025 | 0.78 |
| Attachment loss at baseline | <0.0001\*\* | -0.1±0.036 | 0.0003\*\* | -0.16±0.035 | <0.0001\*\* |
| Treatment group (Placebo as reference) |  |  |  |  |  |
| Control | 0.045\* | -0.03±0.07 | 0.11 | -0.03±0.076 | 0.17 |
| Low | 0.1±0.079 | 0.1±0.076 |
| Medium | 0.1±0.080 | 0.2±0.076 |
| High | 0.01±0.085 | 0.03±0.082 |
| \*p<0.05  \* \*p<0.01 |  |  |  |  |  |

The univariate test showed that attachment loss at baseline (p<0.001) and treatment groups (p=0.045) were significantly associated with change in attachment loss. In multivariate regression, attachment loss at baseline was significant (-0.1±0.036, p<0.0001), which indicated that if attachment loss at baseline increase by 1mm, attachment loss will decrease by 0.1mm on average while holding other variables constant. Treatment group was not associated with change in attachment loss significantly (p=0.11). We detected an outlier (studentized residual=-0.326086956). After this outlier was removed, the result still showed that only attachment loss at baseline was significant(p<0.0001) and treatment group was not significant(p=0.17). As for change in pocket depth, the univariate test showed that treatment, gender and pocket depth at baseline were significantly associated with the outcome (treatment: p=0.09, gender: p=0.027, pocket depth: p=0.04). However, when multivariate regression was performed, no variables were significant (Table 3). No outliers were detected.

**Conclusions:** In the population studied at midwestern dental research clinic, this new gel treatment did not help release the attachment loss and pocket depth. However, there were many improvements that could be made in future. First, this study has small number of patients. Dropout rate (26.2%) is high and may influence the result. If clinicians still want to test this treatment, more participants should be recruited to have higher power. Second, we did not know the missing reason for those participants who did not show up at one-year visit. If no return because their gum became healthier or worse after treatment, the analysis will not be very validated because missing not at random happened. Third, the results showed that gender was associated with missing status (p= 0.003), which indicated that females were more likely to return at one-year visit.

Table 3 Change in pocket depth loss by treatment groups and covariates

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristics** | | **Change in Pocket depth** | | | |
|  | | P-value in univariate test | Regression coefficient in multivariate regression | | P-value in multivariate regression |
| Gender (Female as reference) | | 0.027\* | 0.09±0.058 | | 0.13 |
| Race (Non-white as reference) | | 0.58 | 0.07±0.087 | | 0.41 |
| Age | | 0.46 |  | | 0.23 |
| Smoker (Non-smoker as reference) | | 0.94 | 0.02±0.058 | | 0.79 |
| Sites | | 0.63 | -0.003±0.0026 | | 0.25 |
| Pocket depth at baseline | | 0.04\* | -0.1±0.062 | | 0.072 |
| Treatment group (Placebo as reference) | |  |  | |  |
| Control | | 0.090 | 0.05±0.081 | | 0.11 |
| Low | | 0.2±0.082 | |
| Medium | | 0.1±0.083 | |
| High | | 0.02±0.089 | |
| \* p<0.05 |  |  |  |  |  |

Link to Code

**<https://github.com/BIOS6624-UCD/bios6624-zhwr7125/tree/master/Project0>**

It is in the code folder called “[SAS 0910.sas](https://github.com/BIOS6624-UCD/bios6624-zhuan043/blob/master/Project0/Code/SAS%200910.sas)”