

Analysis of a Clinical Trial for a new drug Luxuriant

Abstract

A known issue in older men is the loss of hair (baldness) and whilst many treatments exist to combat this, results in which this succeeds vary greatly. We investigate a recent clinical trial of three drugs (two pre-existing and a new one) and a placebo with the aim to determine the effects of the new drug (Luxuriant) for the treatment of hair loss (baldness) in men. In our exploration of the data we found that the new drug indeed has an effect beyond a placebo treatment. However in comparison to the other drugs on the market, Luxuriant lies on the lower end of effectiveness. The relation of age to hair growth, moreover, is statistically insignificant in relation to respective treatment groups.

Introduction

The clinical test data consists of 4 categories of hair length for each of the 4 treatments, as well as the ages of the respective participants. All subjects have shown previous signs of baldness and presented shaved to the trial.

We will firstly compare luxuriant against a placebo in order to investigate whether the new drug has a significantly effect on increasing hair growth. Following this we will examine the new drug against two pre-existing treatments (HairyGoodness & BaldBeGone) on participants to determine the strength of the new treatment in relation (if it is more effective). Lastly, we shall consider a possible connection between age and hair length in all treatment groups

Analysis description

Prior to any analysis we look at the data at hand and observe the summaries. Note that we convert measurements from inches to millimeters at the beginning. From the summary output, we clearly see that the spread of the lengths in each treatment group differs substantially, and as such, we must ensure we take this into account in the analysis (such as in t-tests below). We also consider the distributions of the variables noting that some variables are not normal.

Next, we modify our data so that we drop the age columns (we are left with just the four treatments and hair growth) and then modify again to obtain two columns: one for type of treatment and one for the corresponding. Recall that we want to know how the new drug compares to the placebo. We consider the same modification but only including the placebo and luxuriant treatment, as well as creating a box plot, and again noting the difference in

spread. We next perform a Welch's t-test with an α level of 0.05. Similarly, we next compare the new treatment against the two former drugs at the same α level using again a Welch's t-test. Using the data with all 4 methods to treat hair loss combined in one column, we plot a box plot to visually investigate how each differs from one another. We perform, lastly, a simple linear regression for treatments and age (in treatment group). This allows us to statistically infer the type (strong/weak, positive or negative) of the linear relation.

Results

From the summary we find that means and standard deviations both differ based on treatments, with the placebo having the lowest expected growth rate after one month.

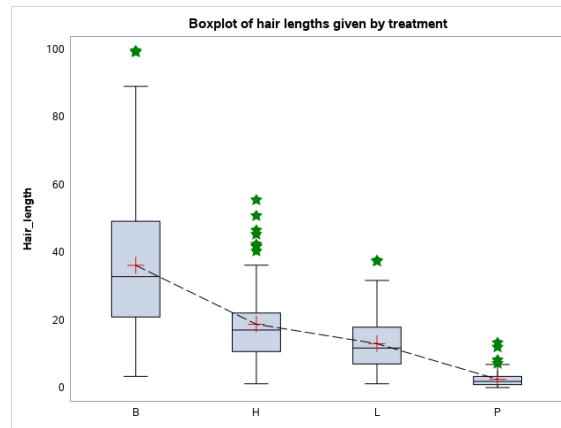
Treatment	Average Hair growth	Standard deviation
Placebo	2.48 mm	2.40 mm
Luxuriant	13.00 mm	7.52 mm
HairyGoodness	18.74 mm	11.02 mm
BaldBeGone	36.15 mm	19.74 mm

We can indeed deduce, based on the Welch's t-test that since the associated p-value is <0.0001 that we are able to reject our null hypothesis that both treatments have the same effect. Meaning that average the hair growth using the Luxuriant drug was 10.5144 mm more than for the group using the placebo. Luxuriant thus has an effect on hair growth (see Figure [1] in Appendix for associated box plot).

Now we investigate how the new treatment compared to the other two on the market. We once again perform Welch's t-test for Luxuriant against HairyGoodness and BaldBeGone, with null hypothesis being that both treatments have the same mean effect and alternative H being that one is more effective (with alpha level of 0.05). Note that overall we will have introduced an error of size $3*0.05 = 0.15=15\%$ since we did not use an ANOVA test.

Treatments	F-value	P-value	Result
Luxuriant - HairyGoodness	2.14	0.0002	H. on average 5.74 mm longer than L.
Luxuriant - BaldBeGone	6.88	0.0001	B. on average 23.15 mm longer than L.

This can be more clearly visualized using a box plot:



Box plot for the different treatments with respect to hair growth (stars are outliers)

We now look at the regression models for each treatment group and their ages. For the placebo and the HairyGoodness drug we observed a fanning out in residuals vs. Predicted values and a curvy line on the QQ-plot. Both indicate of non-normality of the data. We look therefore at the correlations which indicate (using Spearman's correlation coefficient due to non-normal nature, see for example [4]). In both cases we obtain a weak negative value along with insignificant p-values.

For Luxuriant we overall found that <1% of the data could be described using the model (with an ANOVA p-value of ~ 0.9). The only significant coefficient appeared to be the intercept (=13.5). Similarly for BaldBeGone, we obtained a low value ($R^2=0.01$) suggesting that the model is not able to describe the data. The intercept is significant (=51.46).

To conclude, no statistically significant link can be given between each of the pairs (see figures [3] for plots).

Discussion

Overall, we have found that Luxuriant has an effect on the growth of hair compared to the placebo. Observing the effect with regards to the other two drugs already on the market, in particular against the BaldBeGone treatment, the effectiveness of Luxuriant is much less since we find that the average growth differs by roughly 23 mm. No relevancy of age can be observed with hair length.

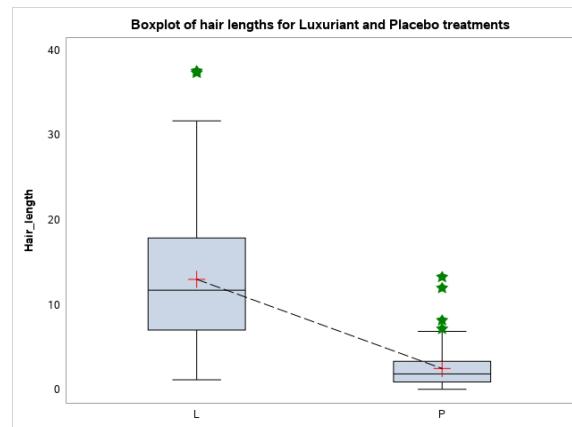
Improvements to this trial could have involved recording participants medical history since (Whiting, D. A. (1998)) noted that the growth of hair “is under complex genetic and hormonal control”. (I.e., some could be affected differently due to underlying conditions compared to those who do not). But also diet, disease or other factors could influence the data collected in the trial. Ingredients in the drugs could have been further analysed to single out those which improve hair growth as well.

Appendix

References and Code:

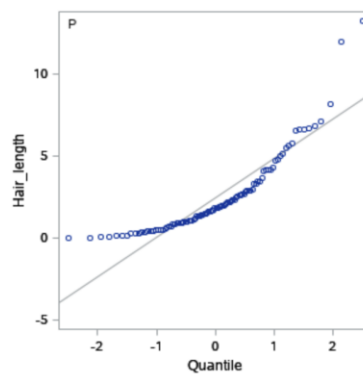
Whiting, D. A. (1998). *Male pattern hair loss: current understanding*. International journal of dermatology, 37(8), 561-566.

[1]



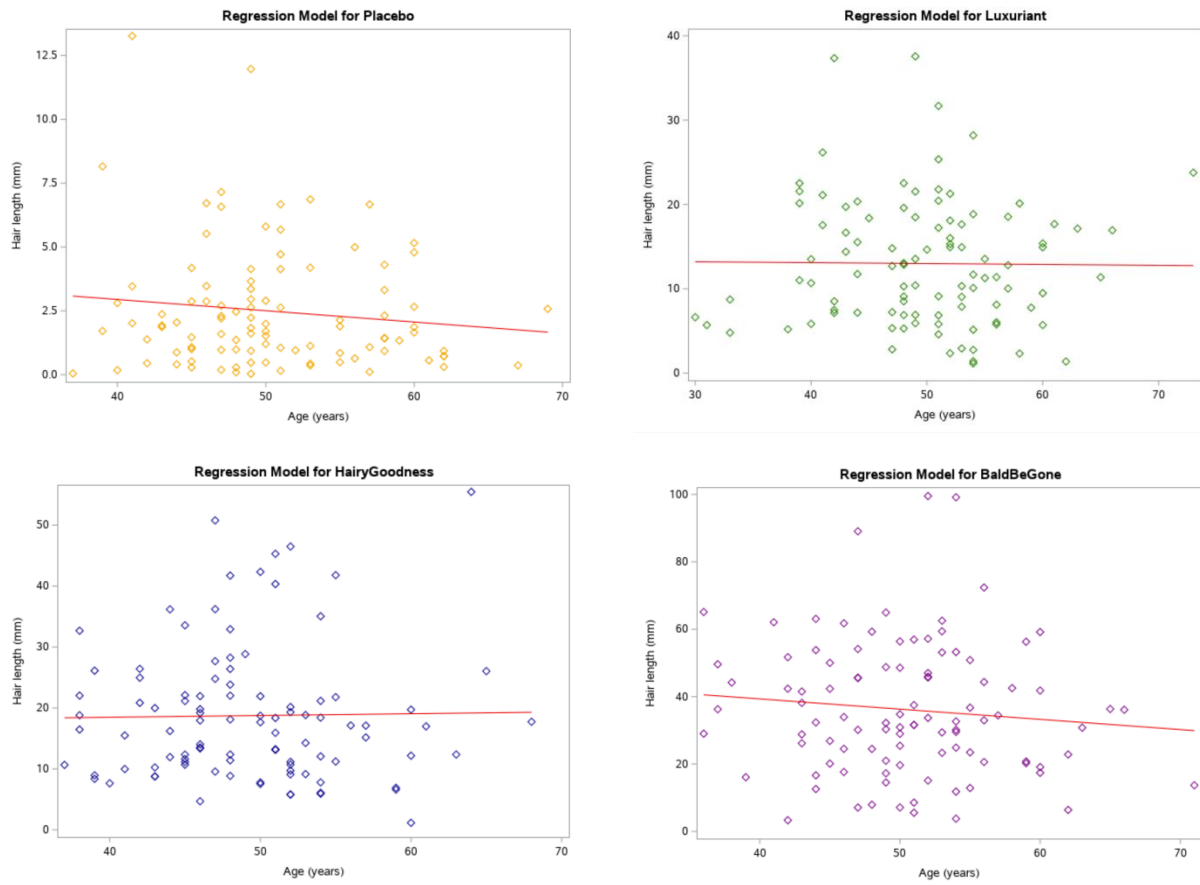
Box plot for Luxuriant treatment against the placebo.

[2]



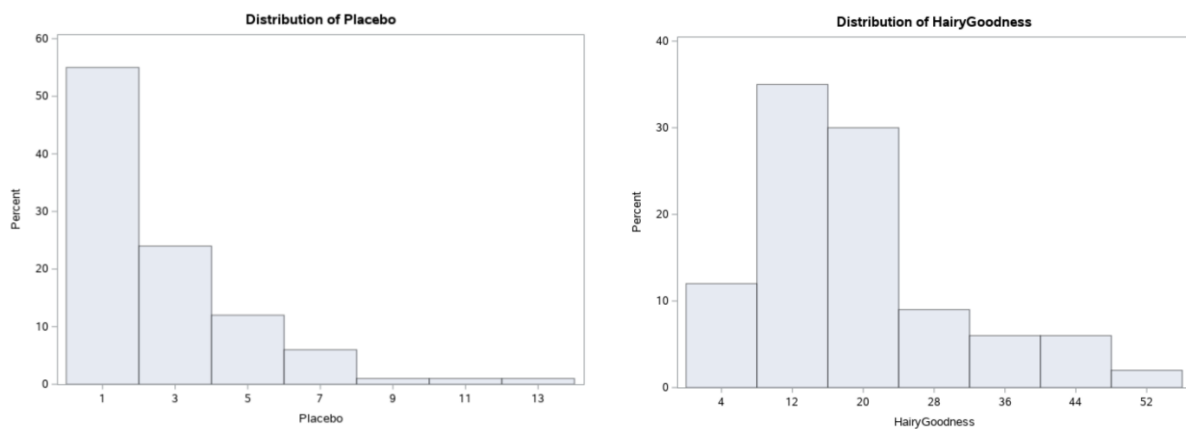
QQ plot for Placebo treatment: clearly non-normal.

[3]



Scatterplots of treatments against respective ages with regression lines. Note that the slopes appear close to zero or are slightly negative.

[4]



Skewed distribution of Placebo and HairyGoodness hair lengths (non-normal).

SAS Code:

```
/* Import data/ read in file: */  
FILENAME REFFILE '/home/u62665966/sasuser.v94/NewFolder/Baldy.csv';  
  
PROC IMPORT DATAFILE=REFFILE  
    DBMS=CSV  
    OUT=baldy.IMPORT;  
    GETNAMES=YES;  
RUN;  
  
/* View the whole data set: */  
proc print data=baldy.IMPORT (obs=100);  
  
run;  
  
/* -----  
--- */  
  
/* Change from inches to mm: (1inch == 25.4mm)*/  
  
DATA baldy.IMPORT_inMM;  
SET baldy.IMPORT;  
Luxuriant=Luxuriant*25.4;  
Placebo=Placebo*25.4;  
HairyGoodness=HairyGoodness*25.4;  
BaldBeGone=BaldBeGone*25.4;
```

```
RUN;

/* -----
--- */

/* From now on use this data set for further analysis:  baldy.IMPORT_inMM */

/* -----
--- */

/* Quick summary: */

PROC UNIVARIATE DATA=baldy.IMPORT_inMM;

/* By hair growth: */
VAR Luxuriant;
VAR Placebo;
VAR HairyGoodness;
VAR BaldBeGone;

/* By age: */
VAR AgeLuxuriant;
VAR AgePlacebo;
VAR AgeHairyGoodness;
VAR AgeBaldBeGone;

RUN;
```

```

/* Means, stdevs and ranges:

    Lux mean = 12.99, std = 7.52,
    Placebo mean 2.485, std = 2.40,
    HairyG mean = 18.74, std = 11.02,
    BaldBeG mean = 36.152, std = 19.74

    AgeL: age range (30-73),
    AgeP: age range (37-69),
    AgeH: age range (37-68),
    AgeB: age range (36-71).

*/

/* How are the variables distributed? */

proc univariate data=baldy.IMPORT_inMM;
    histogram;
run;

/* Although the treatment outcomes do not all follow a normal distribution, the ages
for the participants appears to be normally distributed. */

/* -----
--- */

/* Modify data set to a new one: */

```



```
/* Here we create a new column containing all methods and their corresponding  
   hairlengths */
```

```
data baldy.import_Methods;  
    set baldy.IMPORT_inMM;  
    method = 'L'; Value=Luxuriant;output;  
    method = 'B'; Value=BaldBeGone;output;  
    method = 'H'; Value=hairygoodness;output;  
    method = 'P'; Value=placebo;output;  
    keep method value;  
run;
```

```
/* Rename method to treatments and value to hair length */
```

```
DATA baldy.import_Methods;  
SET baldy.import_Methods;  
RENAME method=Treatment;  
RENAME value=Hair_length;  
RUN;
```

```
/* Sort the data set by model (ascending) */
```

```
proc sort data=baldy.import_Methods  
    out=baldy.import_Methods;  
    by treatment;  
run;
```

```
/* -----  
--- */
```

```
/*
```

Questions to answer:

- 1) Is there an effect of Luxuriant above and beyond the placebo (above)
- 2) Is Luxuriant more effective than the existing treatments on the market
- 3) Is age relevant to any effect?

```
/*
```

```
/* -----  
--- */
```

```
/* We need to firstly look at the spread of Lux against the placebo. Consider  
the
```

```
    boxplot of the two treatments: we will check if normality and simialr spre  
ad hold
```

```
    true: */
```

```
/* Note also : Among moderate or large samples, a violation of normality may  
still
```

```
    yield accurate p values */
```

```
data baldy.import_Methods2;
```

```
    set baldy.IMPORT_inMM;
```

```
    method = 'L'; Value=Luxuriant;output;
```

```
    method = 'P'; Value=placebo;output;
```

```
    keep method value;
```

```

run;

/* Rename method to treatments and value to hair length */
DATA baldy.import_Methods2;
SET baldy.import_Methods2;
RENAME method=Treatment;
RENAME value=Hair_length;
RUN;

/* Sort the data set by model (ascending) */
proc sort data=baldy.import_Methods2
    out=baldy.import_Methods2;
    by treatment;
run;

/* Create a boxplot: */

title "Boxplot of hair lengths for Luxuriant and Placebo treatments";
proc sgplot data=baldy.import_Methods2 noautolegend;
    vbox Hair_length / category=Treatment connect=mean connectattrs=(color=black
pattern=mediumdash thickness=1)
                                meanattrs=(symbol=plus color=red size=20)
                                lineattrs=(color=black)
                                medianattrs=(color=black)
                                whiskerattrs=(color=black)
                                outlierattrs=(color=green
symbol=starfilled size=12);
    xaxis display=(noline noticks nlabel);
    yaxis display=(noline noticks) labelattrs=(weight=bold);

```

```

run;

title;

/* Clearly the spread differs vastly -> assume non-equal std:
   H0: no difference in hair growth
   H1: there is a difference in hair growth (L>P)
   */

/* perform Welch's t-test: */
PROC TTEST DATA=baldy.import_Methods2 ALPHA=.05;
    VAR Hair_length;
    CLASS Treatment;
RUN;

/* Notes: Placebo distribution is skewed to the left (close to zero hair growth) -
           does not resemble a normal distribution compared the graph for Luxuriant.

           (unequal std): Satterthwaite 95% CI for mean is (8.9499, 12.0790), i.e.,
           on average the hair growth using a placebo drug was 10.5144mm less than
           for the group using the new drug Luxuriant.

           Since  $p < 0.0001$  is less than our chosen significance level  $\alpha = 0.05$ , we
           can
           reject the null hypothesis: we conclude that indeed hair growth under luxuriant
           is statistically different (ie 'better' for growth) than the placebo. */

```

```

/* -----
--- */

/* Q2): */

/* -----
--- */

/* H0: both treatments have similar effect of hair growth (no difference)
   H1: one treatment outperforms the other */
data baldy.import_TtestLH;
    set baldy.IMPORT_inMM;
    method = 'L'; Value=Luxuriant;output;
    method = 'H'; Value=HairyGoodness;output;
    keep method value;
run;

/* Rename method to treatments and value to hair length */
DATA baldy.import_TtestLH;
SET baldy.import_TtestLH;
RENAME method=Treatment;
RENAME value=Hair_length;
RUN;

/* perform Welch's t-test: */
proc ttest data=baldy.import_TtestLH ALPHA=.05;
    class Treatment;
    var Hair_length;
run;

/* Although the QQ-plots appear to not resemble a straight line, p-value may
still be

    accurate (test robust to non-normal data (see comment from before L vs P))

```

F-value=2.14, p-value=0.0002 -> look at unequal in 2nd table p <.0001
Reject H0. There is indeed a stat. sig. difference in mean
(on average hair lengths are 5.74mm longer using HairyGoodness than those
measured under the Luxuriant treatment) */

```
/* -----  
--- */
```

```
/* H0: both treatments have similar effect of hair growth (no difference)  
   H1: one treatment outperforms the other */
```

```
data baldy.import_TtestLB;  
    set baldy.IMPORT_inMM;  
    method = 'L'; Value=Luxuriant;output;  
    method = 'B'; Value=BaldBeGone;output;  
    keep method value;  
run;  
proc ttest data=baldy.import_TtestLB ALPHA=.05;  
    class method;  
    var value;  
run;
```

```
/* The QQ-plots appear to be roughly normal.
```

F-value=6.88, p <.0001 -> look at unequal in 2nd table p <.0001
Reject H0. There is indeed a stat. sig. difference in mean
(on average hair lengths are 23.15mm longer using BaldBeGone than those
measured under the Luxuriant treatment) */

```

/* -----
--- */

/* Run the boxplot: */

title "Boxplot of hair lengths given by treatment";
proc sgplot data=baldy.import_Methods noautolegend;
    vbox Hair_length / category=Treatment connect=mean connectattrs=(color=black
pattern=mediumdash thickness=1)
                                meanattrs=(symbol=plus color=red size=20)
                                lineattrs=(color=black)
                                medianattrs=(color=black)
                                whiskerattrs=(color=black
)
                                outlierattrs=(color=green
symbol=starfilled size=12);
    xaxis display=(noline noticks nolabel);
    yaxis display=(noline noticks) labelattrs=(weight=bold);
run;
title;

/* Clearly the distributions of hair length are very different, (violates similar
spread condition, see also the differences in std!!) As seen in the tests
conducted*/

/* -----
--- */

/* 3) Is age relevant to any effect? */

```

```

/* Firstly, let us view scatterplots: */

/*scatterplot with regression line*/
proc sgplot data=baldy.IMPORT_inMM noautolegend;
    title 'Regression Model for Placebo';
    xaxis label='Age (years)';
    yaxis label='Hair length (mm)';
    reg y=Placebo x=AgePlacebo /
    lineattrs=(color=red thickness=1)
    markerattrs=(color=orange size=7px symbol=diamond);
run;

proc sgplot data=baldy.IMPORT_inMM noautolegend;
    title 'Regression Model for Luxuriant';
    xaxis label='Age (years)';
    yaxis label='Hair length (mm)';
    reg y=Luxuriant x=AgeLuxuriant /
    lineattrs=(color=red thickness=1)
    markerattrs=(color=green size=7px symbol=diamond);
run;

proc sgplot data=baldy.IMPORT_inMM noautolegend;
    title 'Regression Model for HairyGoodness';
    xaxis label='Age (years)';
    yaxis label='Hair length (mm)';
    reg y=Hairygoodness x=Agehairygoodness /
    lineattrs=(color=red thickness=1)
    markerattrs=(color=darkblue size=7px symbol=diamond);

```



```

run;

proc sgplot data=baldy.IMPORT_inMM noautolegend;
    title 'Regression Model for BaldBeGone';
    xaxis label='Age (years)';
    yaxis label='Hair length (mm)';
    reg y=Baldbegone x=Agebaldbegone /
    lineattrs=(color=red thickness=1)
    markerattrs=(color=purple size=7px symbol=diamond);
run;

proc sgscatter data=baldy.IMPORT_inMM;
    plot Placebo*AgePlacebo Luxuriant*AgeLuxuriant HairyGoodness*AgeHairygood
    ness BaldBeGone*AgeBaldbegone/ columns= 1 ;
run;

/* Below: looks like weak link between ages and hair length after treatment*/

/* ##### */

/* Investigate stitistically - is p-value signifcant? */

ods graphics on;

proc reg data =baldy.import_inmm alpha = 0.05 plots(only)=(diagnostics residu
als fitplot observedbypredicted);
    model Placebo = AgePlacebo/;
run;

ods graphics off;

/*ANOVA p-value = 0.2339, R-Square 0.0144 -> model accounts for ~1.4% of dat
a

```

top left plot: fanning out: increasing variability in model, qq-plot: not normal

-> assumptions violated */

/* Spearman test since placebo is heavily skewed to the left: */

```
proc corr data=BALDY.IMPORT_INMM spearman nosimple plots=matrix;
```

```
var AgePlacebo;
```

```
with Placebo;
```

```
run;
```

/* Spearman Correlation Coefficients, N = 100

AgePlacebo vs Placebo ~ -0.06279

p-value = 0.5349*/

/* ##### */

```
ods graphics on;
```

```
proc reg data =baldy.import_inmm alpha = 0.05 plots(only)=(diagnostics residuals fitplot observedbypredicted);
```

```
model Luxuriant = AgeLuxuriant/;
```

```
run;
```

```
ods graphics off;
```

/* ANOVA=0.91, R²=0.0001, Intercept= 13.52, p=0.0082; AgeL = -0.01, p=0.91 */

/* ##### */

```
ods graphics on;
```

```
proc reg data =baldy.import_inmm alpha = 0.05 plots(only)=(diagnostics residuals fitplot observedbypredicted);
```

```
model Hairygoodness = Agehairygoodness/;
```

```

run;

ods graphics off;

/* ANOVE p =0.87, R^2 = 0.0003, Intcept = 17.3, p=0.047; AgeH=0.029, p=0.87
   observe a fanning out and qq plot not normal

           -> assumptions violated      */

proc corr data=BALDY.IMPORT_INMM spearman nosimple plots=matrix;
    var AgeHairyGoodness;
    with HairyGoodness;
run;

/*      Spearman Correlation Coefficients, N = 100
      AgeHairyGoodness vs HairyGoodness ~ -0.06428
      p-value =0.5252
*/

/* ##### */

ods graphics on;

proc reg data =baldy.import_inmm alpha = 0.05 plots(only)=(diagnostics residu
als fitplot observedbypredicted);
    model Baldbegone = Agebaldbegone;
run;

ods graphics off;

/* ANOVA p=0.31, R^2=0.01, intcept=51.46, p=0.0009; AgeB=-0.3, p = 0.31
   No patterns in Res vs Pred. value plot, follows diag on qq plot.

```