The Two-Factor Mixed Model

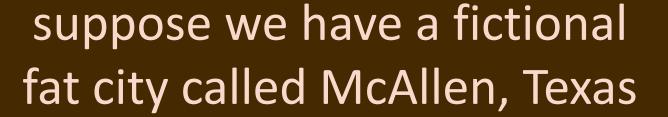




Nomenclature

- Two-Factor
 - Let F and R be our factors and note there are two
- Mixed Model
 - F is a fixed factor
 - R is a random factor







We want to test a weight loss cake

fattest city in america











wallethub.com

https://wallethub.com > edu > fattest-cities-in-america

Most Overweight and Obese Cities in the U.S. - WalletHub

Mar 13, 2023 — **Fattest Cities** in the **U.S.**; 1, McAllen-Edinburg-Mission, TX, 85.93; 2, Memphis, TN-MS-AR, 84.88; 3, Mobile, AL, 84.52; 4, Knoxville, TN, 84.31 ...



beckershospitalreview.com

https://www.beckershospitalreview.com > 10-most-ove...

10 most overweight US cities - Becker's Hospital Review

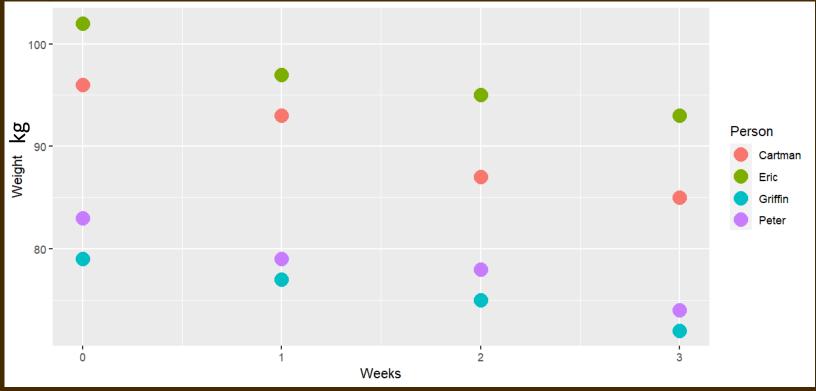
Mar 14, 2022 — McAllen, Texas, is the most overweight and **obese city** in the **U.S.**, according to an analysis by WalletHub, a personal finance website.

Hypothesis testing

- HO: $\mu_0 = \mu_{Cake747}$
 - Cake recipe 747 diet does not cause weight loss
- Ha: $\mu_0 > \mu_{Cake747}$
 - Cake recipe 747 in diet causes significant weight loss



Data



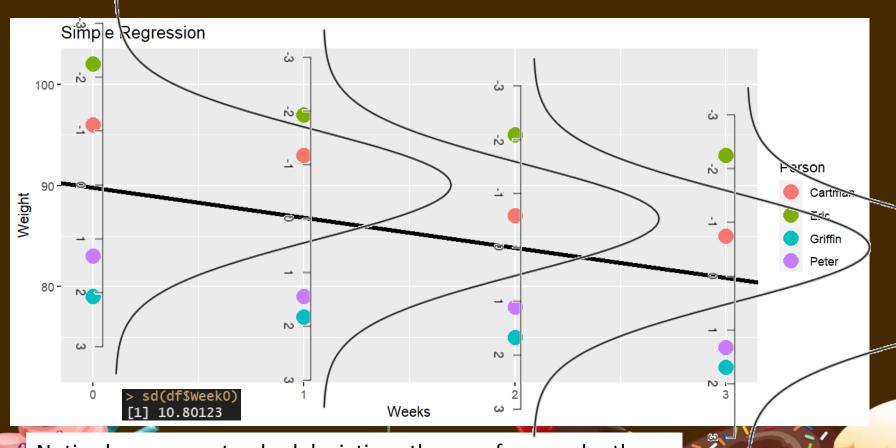


```
library("ggplot2")
Call:
lm(formula = Weight ~ Weeks, data = dfSimpleRegression)
                                                         ggp <- ggplot(dfLong,aes(</pre>
                                                           x=Weeks,
Residuals:
                                                           y=Weight,
   Min
            10 Median
                                                           group=Person))+geom_point(aes(color=Person), size=5)
-10.775 -8.056 -1.325
                         7.219 12.225
Coefficients:
                                                         dfLong.lm <- lm(Weight ~ Weeks, dfLong)</pre>
           Estimate Std. Error t value Pr(>|t|)
                                                         summary (dfLong. 1m)
(Intercept) 92.750
                         5.637 16.453 1.49e-10 ***
                                                        coeff<-coefficients(dfLong.lm)
             -2.975
                         2.058 -1.445
Weeks
                                                         intercept<-coeff[1]
                                                         slope<- coeff[2]
Signif. codes: 0 '***, 0.001 '**, 0.01 '*, 0.05 '.', 0.1
                                                         ggp = ggp + ggtitle("Simple Regression")
                                                         + geom_abline(intercept = intercept, slope = slope, color="red", size=1.5)
Residual standard error: 9.206 on 14 degrees of freedom
Multiple R-squared: 0.1298, Adjusted R-squared: 0.06767
```

F-statistic: 2.089 on 1 and 14 DF, p-value: 0.1704

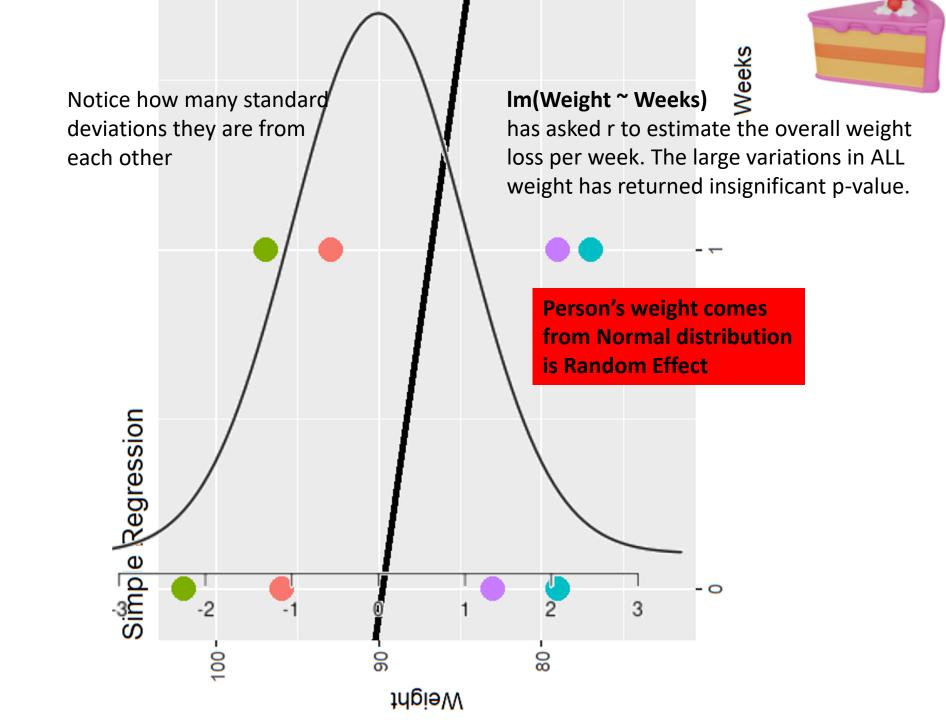


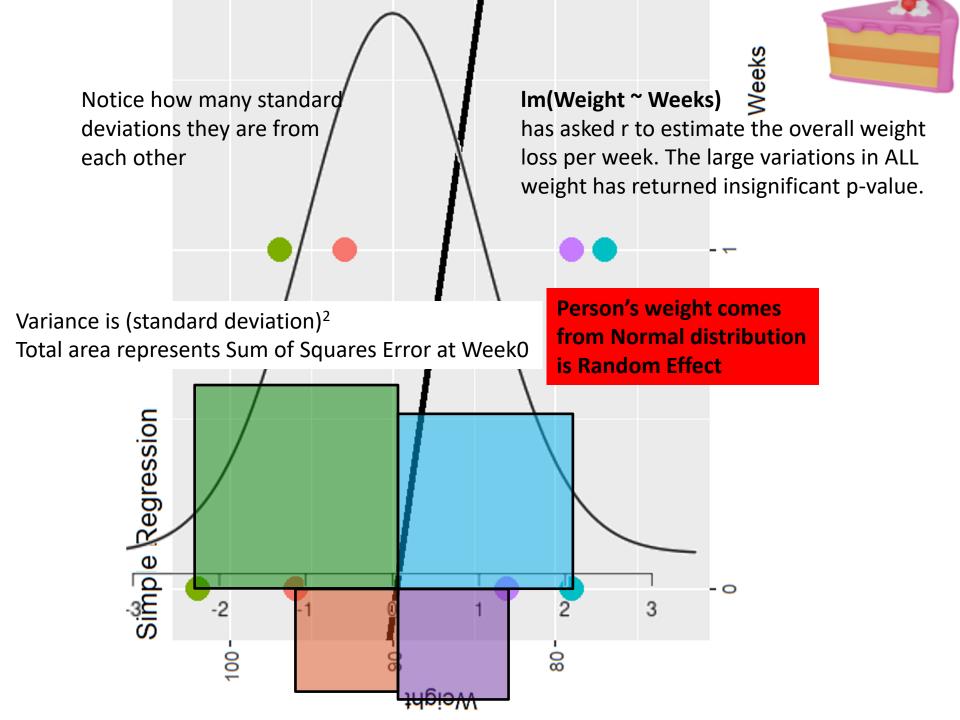
Mistake is the 4 Person randomly selected had different weights



Notice how many standard deviations they are from each other

Simple linear regression is the wrong model to use. Enter **Two-Factor Mixed Model**



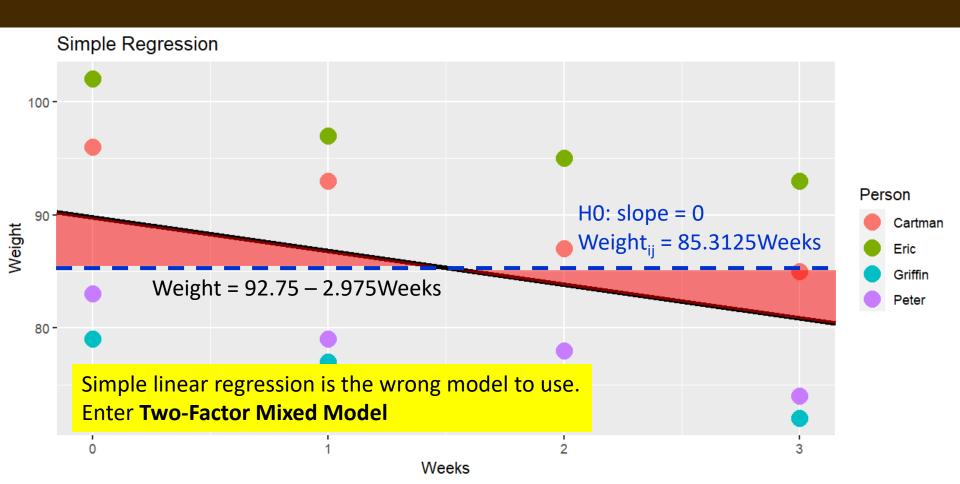


Im(Weight ~ Weeks) has asked R to estimate the overall weight loss per week.

Im has estimated our population mean **weight** before diet to be 92.75kg with slope negative 2.975kg loss per **week** but is insignificant relative to variation in data

It has a null hypothesis that our population mean **Weight** before diet to be 85.3125kg and the slope is zero. That is, any given **Weeks** has an estimated **Weight** of 85.3125kg for any **Person**

The large variations in ALL weight has returned insignificant p-value $0.17 > \alpha$ We conclude that nobody eating Cake747 is losing weight in McAllen, Texas



mean(dfLong\$Weight)

Definitions

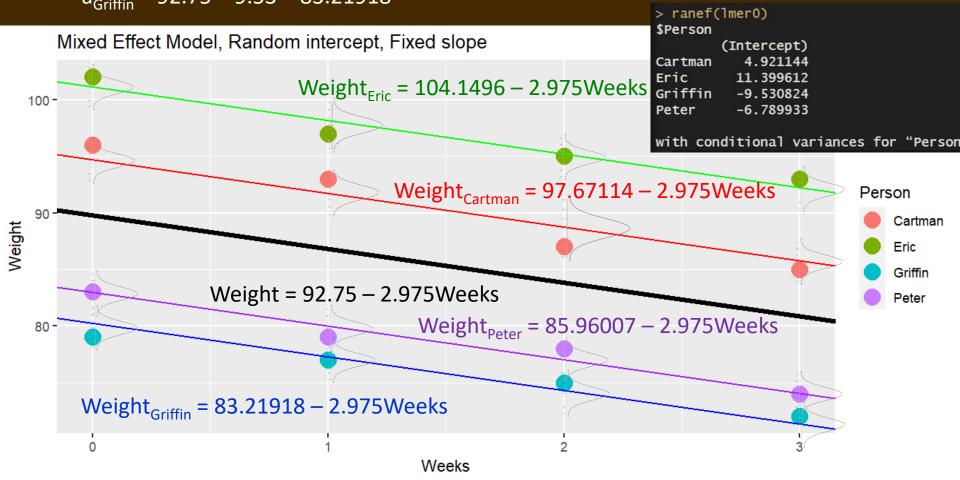
- Fixed effects represent things like the population mean that do not vary. These may represent the population parameters that we like to estimate in, for example, linear regression.
- Random effects represent parameters that can vary between groups of dependent data points. For example, if we do several measurements on the same individual, the mean of these measurements can represent one estimated parameter. Each individual may then have a unique estimate.

```
Linear mixed model fit by REML. t-tests use Satterthwaite's meth
 dfLong.lm <- lm(Weight ~ Weeks, dfLong)</pre>
                                                                             Formula: Weight ~ Weeks + (1 | Person)
                                                                                 Data: dfLong
                                                                             REML criterion at convergence: 66.2
  library(lmerTest)
  lmer0 <- lmer(Weight~Weeks+(1|Person), data=dfLong)</pre>
                                                                             Scaled residuals:
  summary(1mer0)
                                                                                   Min
                                                                                                  Median
                                                                                                                         Max
  ranef(1mer0)
                                                                             -1.53483 -0.73032 -0.01984 0.67606 1.14606
                                                                             Random effects:
                                                                                                    Variance Std.Dev.
                                                                              Groups
                                                                                        Name
Weeks is our fixed effect
                                                                                        (Intercept) 97.359
                                                                              Person
                                                                                                              9.867
                                                                              Residual
                                                                                                      1.294
                                                                                                            1.138
Person is our random effect
                                                                             Number of obs: 16, groups: Person, 4
                                                                                                                                ignificant
1 specifies to use random intercept for Person
                                                                             Fixed effects:
                                                                                          <u>Estimate</u> Std. Error
                                                                                                                    df t value Pr(>|t|)
ranef() give random offset from fixed effect
                                                                                                                          18.61 0.000277 ***
                                                                                                        4.9825 3.1000
                                                                              (Intercept) 92.7500
                                                                                                        0.2544 11.0000 -11.69 1.52e-07 ***
                                                                             Weeks
                                                                                            -2.9750
                                                                             Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' '1
ac <- 4.921144
                                                                             Correlation of Fixed Effects:
ae <- 11.399612
                                                                                    (Intr)
aq < -9.530824
                                                                             Weeks -0.128
ap <- -6.789933
<u>qqp = qqp + qeom_abli</u>ne(intercept = intercept+ac, slope = slope, color="red", size=.5)
ggp = ggp + geom_abl/ine(intercept = intercept+ae, slope = slope, color="green", size=.5)
ggp = ggp + geom_ab/line(intercept = intercept+ag, slope = slope, color="<mark>blue</mark>", size=.5)
ggp = ggp + geom_ab/line(intercept = intercept+ap, slope = slope, color="purple", size=.5)
> ranef(1mer0)
                                                 N / ImerTest / ImerTest-package: ImerTest: Tests in Linear Mixed Effects Models
$Person
          (Intercept)
             4.921144
Cartman
                                                                 ImerTest-package: ImerTest: Tests in Linear Mixed Effects
Eric
            11.399612
Griffin
                                                                 Models
            -9.530824
            -6.789933
Peter
                                                                 In ImerTest: Tests in Linear Mixed Effects Models
with conditional variances for "Person"
                                                                 Description
                                                                          Key Functions and Methods
                                                                                                    Author(s)
                                                                                                            References
                                                                                                                      Examples
                                                               Description
                                                                The ImerTest package provides p-values in type I, II or III anova and summary tables for linear mixed models ( 1mer model fits
                                                                cf. Ime4) via Satterthwaite's degrees of freedom method; a Kenward-Roger method is also available via the pbkrtest package.
                                                                Model selection and assessment methods include step, drop1, anova-like tables for random effects (ranova), least-square
                                                                means (LS-means; ls_means) and tests of linear contrasts of fixed effects (contest).
```



Weight_i = $a_i + b^*$ Weeks

 $a_{Peter} = 92.75 - 6.80 = 85.96007$ $a_{Griffin} = 92.75 - 9.53 = 83.21918$ Notice how small the variances are from their own lines The advantage is that the data points are now much closer to the lines, which will result in a much smaller standard error and therefore a smaller p-value.

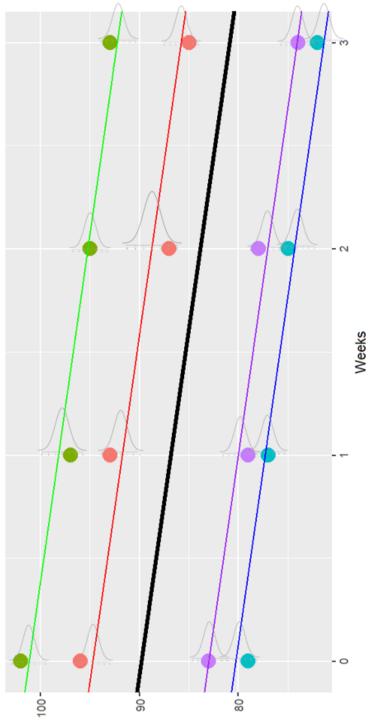


Notice how small the variances are from their own lines Hence the drop in SE and huge drop in SSR

SLR

```
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)
              89.775
                          3.851 23.312 1.33e-12 ***
Weeks
              -2.975
                         2.058 -1.445
                                            0.17
> summary(aov(Weight ~ Weeks, df0))
            Df Sum Sq Mean Sq F value Pr(>F)
Weeks
                                2.089
                                        0.17
                  177 177.01
Residuals
            14 1186
                        84.74
```

2FMM

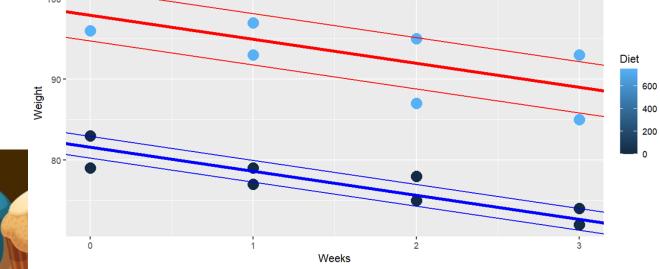


Hypothesis testing



- H0: $\mu_{Cake0} = \mu_{Cake747}$
 - Cake recipe 747 in diet does not cause weight loss compared to cake recipe 0
- Ha: $\mu_{Cake0} > \mu_{Cake747}$
 - Cake recipe 747 in diet causes significant weight loss compared to cake recipe 0

There was a different flatter slope all this time to force a higher Im() pvalue and be reused later in other tests. Can you already guess the answer? Shout it out!



Random intercept & Random Slope

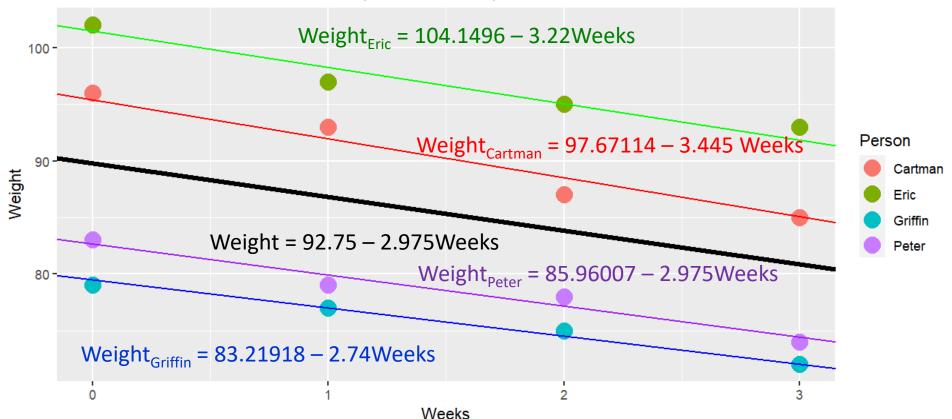
```
# random intercept, fixed slope

lmer0 <- lmer(Weight~Weeks+(1|Person), data=dfLong)
# random intercept, random slope slope

lmer1 <- lmer(Weight~Weeks+(1+Weeks|Person), data=dfLong)
ranef(lmer1)
```

```
$Person
(Intercept) Weeks
Cartman 5.653001 -0.4702121
Eric 11.763864 -0.2462449
Griffin -10.278128 0.4862867
Peter -7.138737 0.2301703
with conditional variances for "Person"
```

Mixed Effect Model, Random intercept, Random slope



- "Weeks" P-Values so far
- Simple Linear Regression
 - **√** 0.17
- Fixed Effect Weeks, Random Effect Person
 - Random Intercept, fixed Slope
 - ✓ 1.52e-07
 - Random Intercept, Random Slope
 - **✓** 0.003013
- Multiple Linear Regression
 - Should not be used since it violate the assumption of independence.
 - the observations are not independent because we have four data points from the same person.





```
dfMissing <- dfLong
dfMissing[9,4] = NA
lmer0 <- lmer(Weight~Weeks+(1|Person), data=dfMissing)
summary(lmer0)</pre>
```

```
Linear mixed model fit by REML. t-tests use Satterthwaite's met Formula: Weight ~ Weeks + (1 | Person)

Data: dfMissing
```

REML criterion at convergence: 63.7

```
Scaled residuals:
```

```
Min 1Q Median 3Q Max -1.47020 -0.75226 0.02032 0.61565 1.10688
```

Random effects:

```
Groups Name Variance Std.Dev.
Person (Intercept) 97.932 9.896
Residual 1.415 1.189
Number of obs: 15, groups: Person, 4
```

Fixed effects:

```
Estimate Std. Error df t value Pr(>|t|)
(Intercept) 92.7500 5.0013 3.1052 18.55 0.000277 ***
Weeks -2.9675 0.2682 9.9989 -11.06 6.25e-07 ***
```

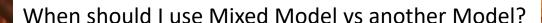
Signif. codes: 0'***'0.001'**'0.01'*'0.05'.'0.1''1

```
Correlation of Fixed Effects:
```

```
(Intr)
Weeks -0.132
```

```
Person Diet Weeks Weight id
1.1
       Eric
             747
                           102
2.1 Cartman
            747
                            96
3.1
                            83
      Peter
4.1 Griffin
                            79
1.2
       Eric
2.2 Cartman
             747
      Peter
                            79
4.2 Griffin
                            NA
       Eric
             747
2.3 Cartman
      Peter
4.3 Griffin
       Eric
             747
                            93
                            85
2.4 Cartman
             747
                            74
      Peter
4.4 Griffin
                            72
```

Repeated Measures ANOVA would have dropped Eric thus reducing statistical power



Imer will run binary outcomes

- that is, dependent variable (Weight) was instead a binary count such as Heads in a coin flipping experiment
- ANOVA assumes dependent variable is continuous.

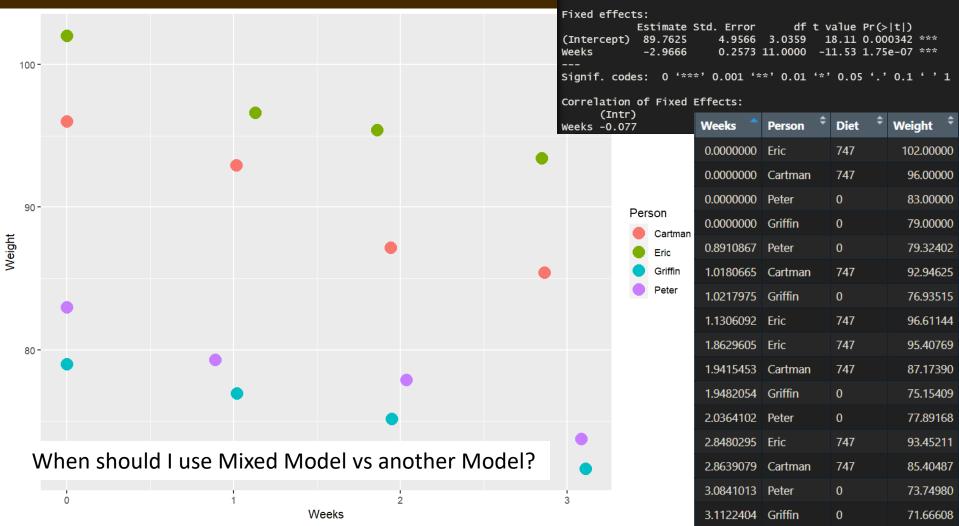


Repeated Measures ANOVA requires measures to be categorical

- That is, Weight measurements need to be on Week0, Week1, ..., Week_n
- Imer will run using data where Weight is measured at any Week $_{\mathbb{R}}$ such as Week0, Week1.618, Week2.718, Week3.14
 - More flexibility in taking measurements
 - Simple Linear Regression will also run any real x-axis

Imer can use any real x-axis

Linear mixed model fit by REML. t-tests use Satterthwaite's met Formula: Weight ~ Weeks + (1 | Person) Data: dfAnyReal REML criterion at convergence: 66.2 Scaled residuals: Median -1.53850 -0.73703 -0.02012 0.67110 1.15688 Random effects: Variance Std.Dev. Groups Person (Intercept) 97.364 Residual 1.294 1.138 Number of obs: 16, groups: Person, 4



Simple Linear Regression will also run any real x-axis

```
> summary(lm(Weight ~ Weeks, dfAnyReal))
Ca11:
lm(formula = Weight ~ Weeks, data = dfAnyReal)
Residuals:
    Min
            10 Median
                            3Q
                                   Max
-10.577 -7.991 -1.323 7.389 12.423
Coefficients:
           Estimate Std. Error t value Pr(>|t|)
(Intercept)
             89.577
                         3.253 27.536 <2e-16 ***
             -2.876
                         1.660 -1.733 0.0949 .
Weeks
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
Residual standard error: 8.819 on 26 degrees of freedom
Multiple R-squared: 0.1036, Adjusted R-squared: 0.06908
F-statistic: 3.003 on 1 and 26 DF, p-value: 0.09493
> summary(aov(Weight ~ Weeks, dfAnyReal))
           Df Sum Sq Mean Sq F value Pr(>F)
           1 233.6 233.62
                               3.003 0.0949 .
Weeks
           26 2022.3
Residuals
                       77.78
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

If we only have two Weight measurements per Person

 the linear mixed-effects model with random intercepts will result in the exact same p-value as the repeated measure ANOVA and the paired t-test but only if the repeated measurements have a positive correlation

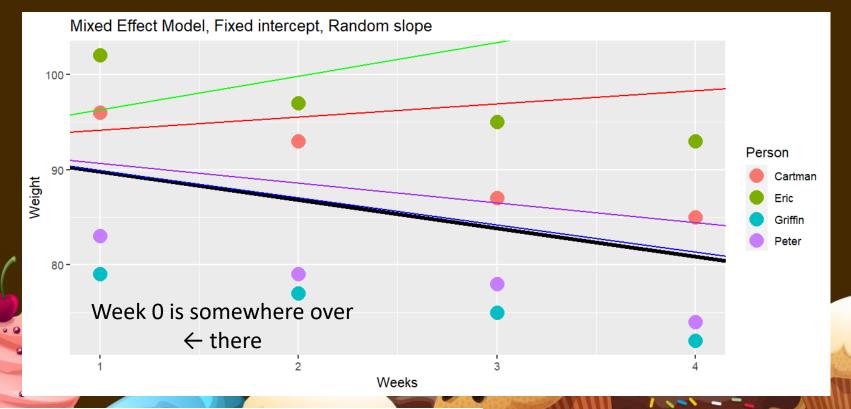


Random Slope only



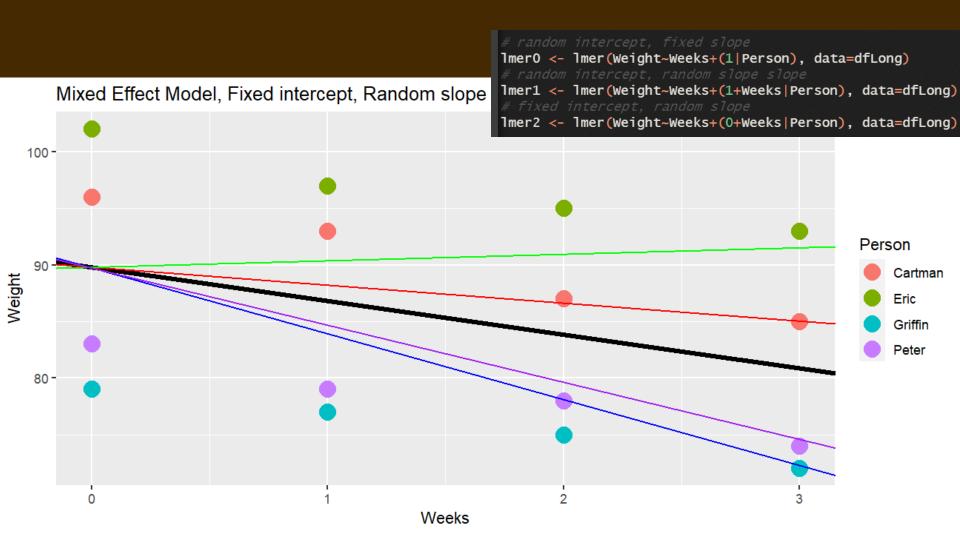
Reshape started Weeks at 1

```
# random intercept, fixed slope
lmer0 <- lmer(Weight~Weeks+(1|Person), data=dfLong)
# random intercept, random slope slope
lmer1 <- lmer(Weight~Weeks+(1+Weeks|Person), data=dfLong)
# fixed intercept, random slope
lmer2 <- lmer(Weight~Weeks+(0+Weeks|Person), data=dfLong)</pre>
```



Random Slope, Fixed intercept

- This looks wrong
- Transform our data to use Fixed Intercept, Random Slope





```
weightLoss <- df
for(r in 1:4){
  for(c in 6:3) {
    weightLoss[r, c] = weightLoss[r, c] - weightLoss[r,3]
  }
}</pre>
```

Get difference from right to left is most efficient

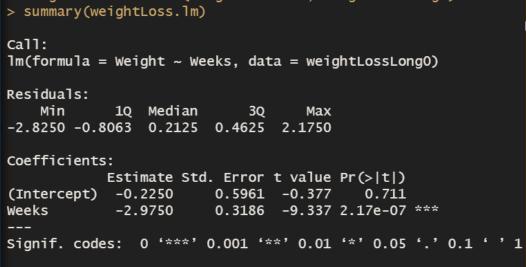
^	Person [‡]	Diet [‡]	Week0 [‡]	Week1 [‡]	Week2 [‡]	Week3 [‡]
1	Eric	747	0	-5	-7	-9
2	Cartman	747	0	-3	-9	-11
3	Peter	0	0	-4	-5	-9
4	Griffin	0	0	-2	-4	-7



Random Slope Fixed intercent

> weightLoss.lm <- lm(Weight ~ Weeks, weightLossLong0)

Running SLR on Weight Loss would have worked from the start



ent

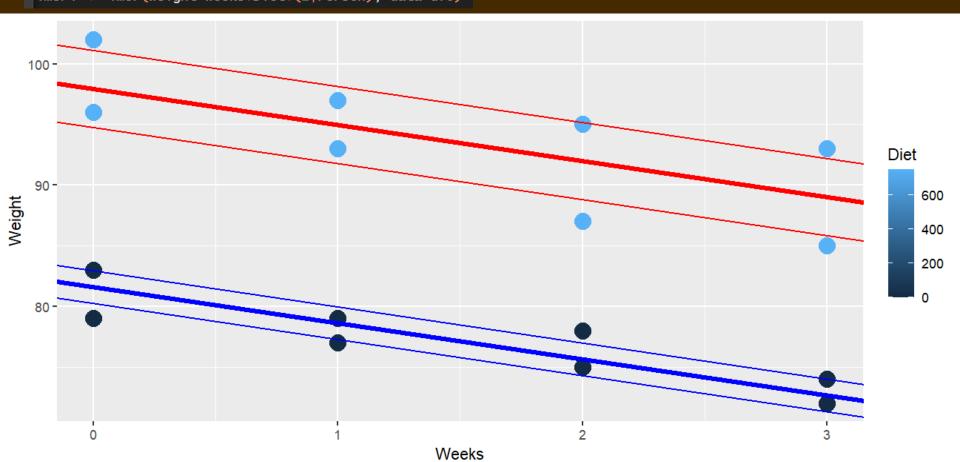


Weeks



```
# random intercept, fixed slope
lmer0 <- lmer(Weight~Weeks+(1|Person), data=df0)
# random intercept, random slope slope
lmer1 <- lmer(Weight~Weeks+(1+Weeks|Person), data=df0)
# fixed intercept, random slope
lmer2 <- lmer(Weight~Weeks+(0+Weeks|Person), data=df0)
# random intercept + Diet, fixed slope
lmer4 <- lmer(Weight~Weeks+Diet+(1|Person), data=df0)</pre>
```

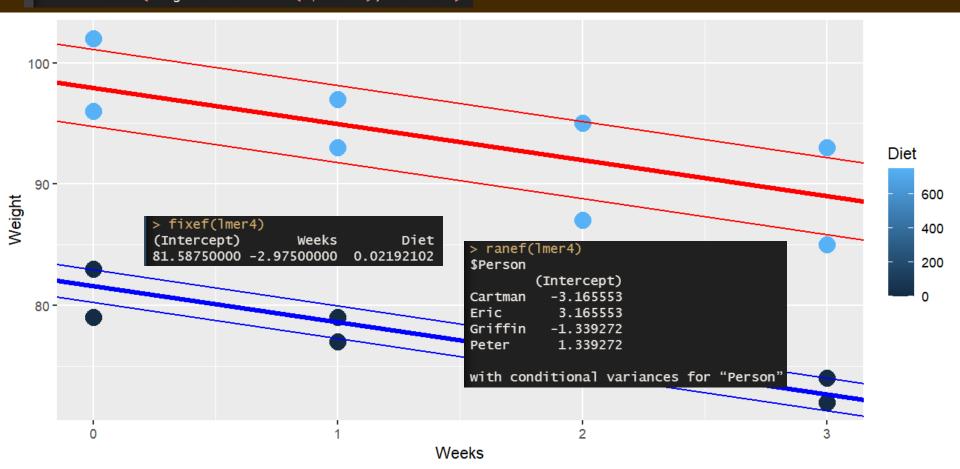
Random Effect is thin line from Thick Fixed Effect line



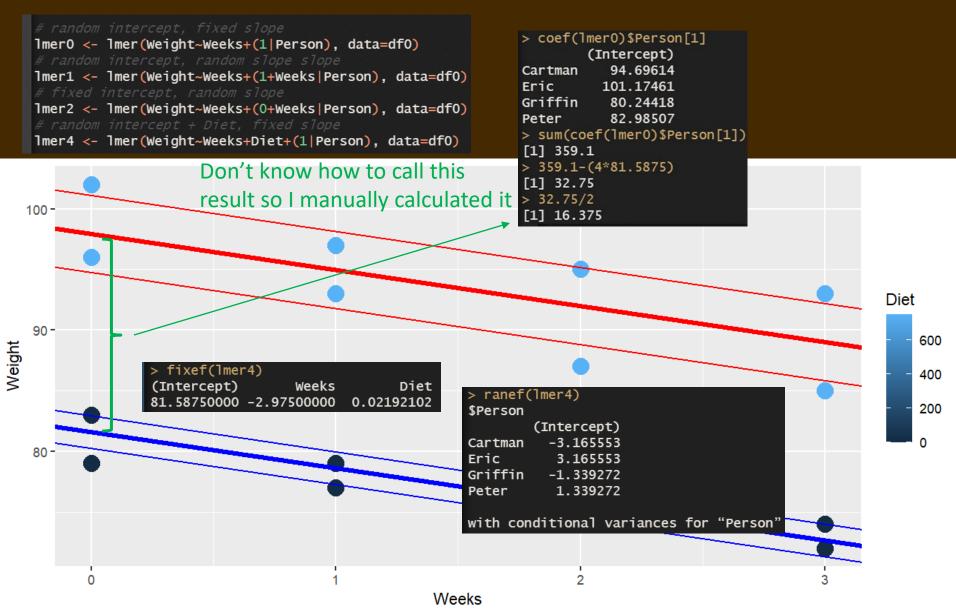


```
# random intercept, fixed slope
lmer0 <- lmer(Weight~Weeks+(1|Person), data=df0)
# random intercept, random slope slope
lmer1 <- lmer(Weight~Weeks+(1+Weeks|Person), data=df0)
# fixed intercept, random slope
lmer2 <- lmer(Weight~Weeks+(0+Weeks|Person), data=df0)
# random intercept + Diet, fixed slope
lmer4 <- lmer(Weight~Weeks+Diet+(1|Person), data=df0)</pre>
```

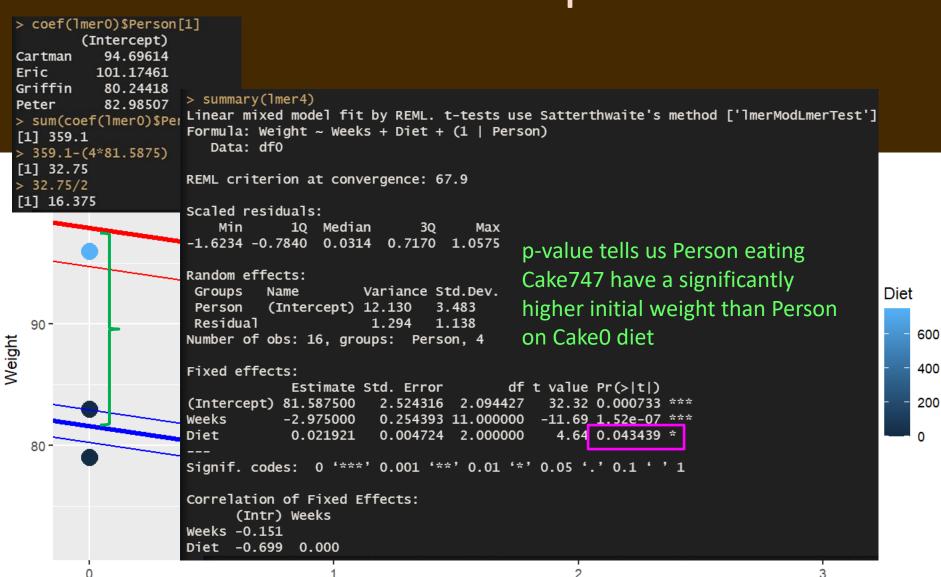
Random Effect is thin line from Thick Fixed Effect line











Weeks

Model with Diet (Random slope)

Is there a significant difference in the Weight loss per Week between the two Diets?

```
# random intercept, fixed slope
Imer0 <- Imer(Weight~Weeks+(1|Person), data=df0)
# random intercept, random slope slope
Imer1 <- Imer(Weight~Weeks+(1+Weeks|Person), data=df0)
# fixed intercept, random slope
Imer2 <- Imer(Weight~Weeks+(0+Weeks|Person), data=df0)
# random intercept + Diet, fixed slope
Imer4 <- Imer(Weight~Weeks+Diet+(1|Person), data=df0)
# random intercept * Diet interaction, fixed slope
Imer5 <- Imer(Weight~Weeks*Diet+(1|Person), data=df0)</pre>
```

Weeks*Diet interaction now allow Diet747 to have different slope from Diet0





Weeks*Diet interaction

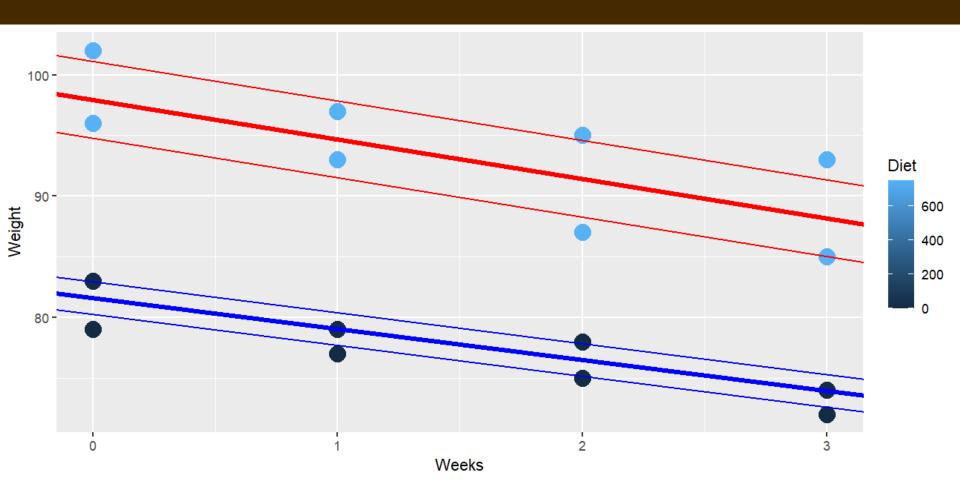
Diet0 has slope of -2.55 Diet747 has slope -2.55 - 0.707 = -3.257p-value of the interaction is not significant. We conclude that the slopes of Diet747 and Diet0 are not significantly different

```
> summary(1mer5)
> summary(lmer4)
                                                                 Linear mixed model fit by REML. t-tests use Satterthwaite's method
Linear mixed model fit by REML. t-tests use Satterthwaite's meth
                                                                 Formula: Weight ~ Weeks * Diet + (1 | Person)
Formula: Weight ~ Weeks + Diet + (1 | Person)
                                                                    Data: df0
   Data: df0
                                                                 REML criterion at convergence: 77.7
REML criterion at convergence: 67.9
                                                                 Scaled residuals:
Scaled residuals:
                                                                      Min
                                                                                10
                                                                                   Median
                                                                                                          Max
    Min
             1Q Median
                                                                 -1.57097 -0.59631 0.03153 0.59333 1.37695
-1.6234 -0.7840 0.0314 0.7170 1.0575
                                                                 Random effects:
Random effects:
                                                                           Name
                                                                                       Variance Std.Dev.
                                                                  Groups
Groups
                      Variance Std.Dev.
                                                                           (Intercept) 12.188
                                                                  Person
Person
          (Intercept) 12.130
                                                                  Residual
                                                                                        1.062
Residual
                       1.294
                                                                 Number of obs: 16, groups: Person, 4
Number of obs: 16, groups: Person, 4
                                                                 Fixed effects:
Fixed effects:
                                                                               Estimate Std. Error
                                                                                                           df t value Pr(>|t|)
             Estimate Std. Error
                                        df t value Pr(>|t|)
                                                                                                              31.835 0.000638
                                                                 (Intercept) <u>80 9500000</u> 2.5427594 2.1558884
(Intercept) 81.587500 2.524316 2.094427
                                             32.32 0.000733 ***
                                                                             -2.5500000 0.3259601 10.0000000
                                                                 Weeks
                                                                                                              -7.823 1.43e-05
          -2.975000 0.254393 11.000000 -11.69 1.52e-07 ***
                                                                                                                4.908 0.033556
Weeks
                                                                 Diet
                                                                              0.0236278 0.0048139 2.1558884
                        0.004724 2.000000
                                                                 Weeks:Diet -0.0011379 0.0006171 10.0000000
                                                                                                               -1.844 0.094989
Diet
            0.021921
                                              4.64 0.043439 *
                                                                 Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Correlation of Fixed Effects:
                                                                 Correlation of Fixed Effects:
      (Intr) Weeks
                                                                            (Intr) Weeks Diet
                                                                            -0.192
Weeks -0.151
                                                                 Weeks
                                                                            -0.707 0.136
                                                                 Diet
Diet -0.699
             0.000
                                                                 Weeks:Diet 0.136 -0.707 -0.192
```

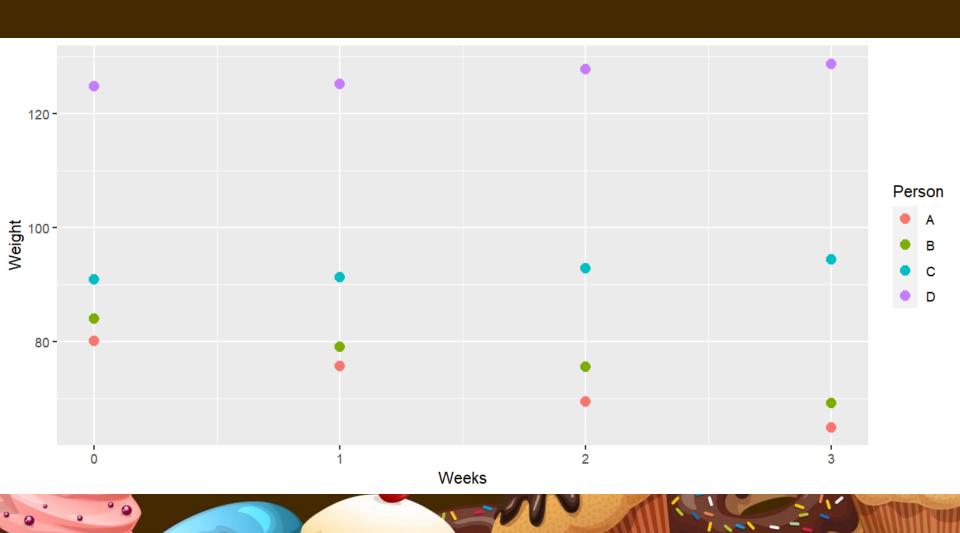


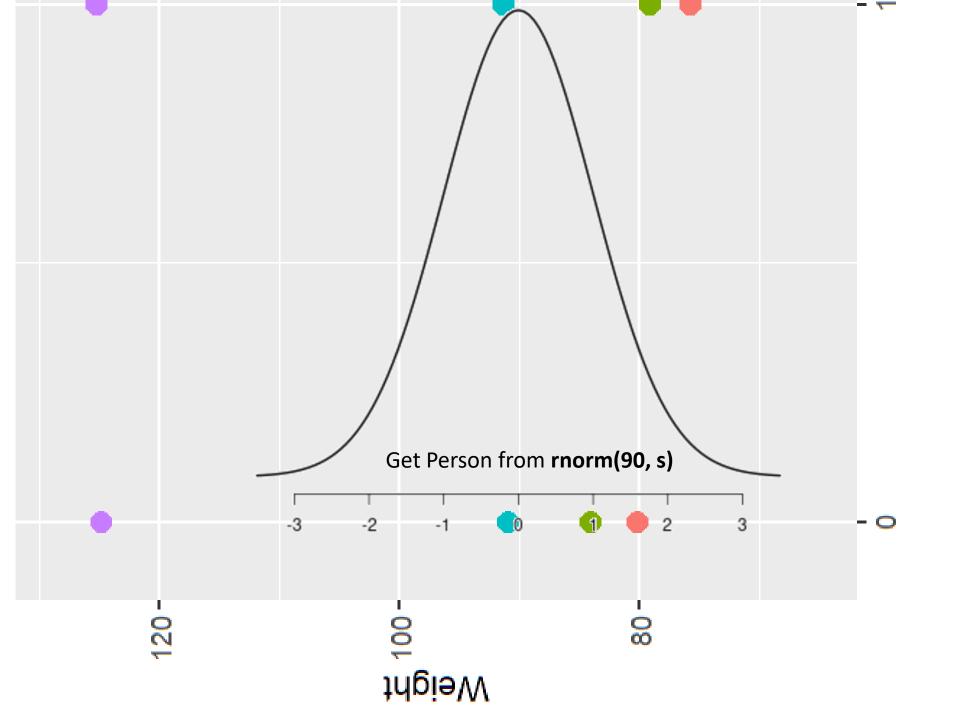
Weeks*Diet interaction

There is no significant difference between average weight loss for Person on Diet with Cake747 and Person on Diet with Cake0 Let's look at a case where there is a significant difference.



Generate Synthetic Data



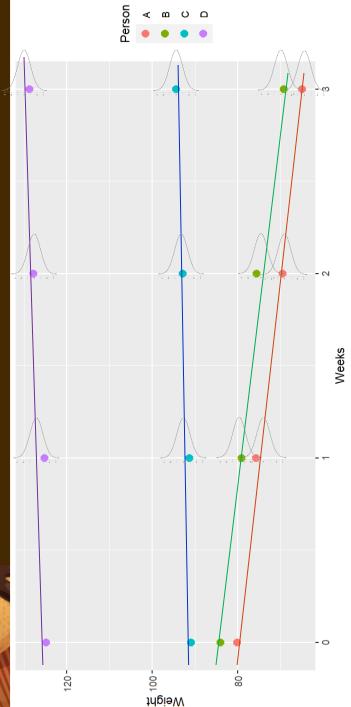


Get Person; from rnorm(90, s)

Calculate predicted Weight_{i,j} at Week_j

Add Gaussian noise to knock predicted weight randomly off its line Weight_{i,j} + rnorm(0, s')





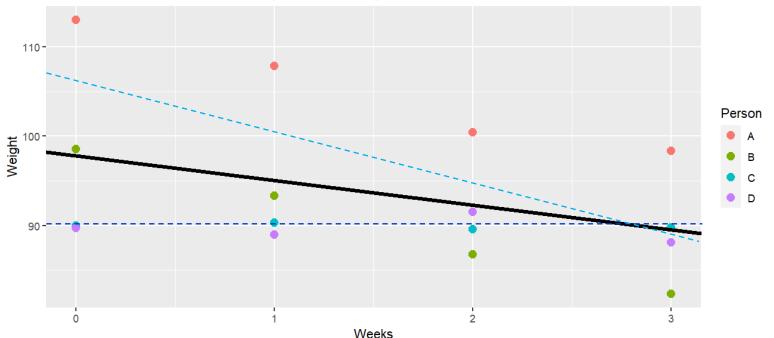
Person{C, D} given CakeO was generated with flat slope.

Person{A,B} given Cake747 was generated with -5 slope (Weeks)

rnorm(mean=90, sd=15) was used, which SLR got wrong due to 15² variation but 2FMM predicted correctly because our two CakeO happens to be generated next to mean. 2FMM averages Weight of WeekO within each Diet group

We expect simple linear regression (on left) to be insignificant due to high variance 15² kg We expect Two-Factor Mixed Model (on right) to have significant Weeks:Diet interaction If you've understood this slide, you've understood the entire presentation

```
Coefficients:
                                                      Fixed effects:
            Estimate Std. Error t value Pr(>|t|)
                                                                                                 df t value Pr(>|t|)
                                                                    Estimate Std. Error
(Intercept)
                          3.203 30.527 3.28e-14 ***
              97.791
                                                      (Intercept) 90.0146054 5.2137050 2.0427617
                                                                                                     17.265
                                                                                                             0.00304 **
Weeks
                                 -1.608
              -2.753
                          1.712
                                             0.13
                                                      Weeks
                                                                  -0.1799600 0.3567269 10.0000000
                                                                                                     -0.504
                                                      Diet
                                                                   0.0208194
                                                                              0.0098705
                                                                                        2.0427617
   synth0.lm <- lm(Weight ~ Weeks, synth0)</pre>
                                                      Weeks:Diet -0.0068881 0.0006754 10.0000000 -10.199 1.33e-06 ***
   summary(synth0.1m)
                                                       lmer5 <- lmer(Weight~Weeks*Diet+(1|Person), data=synth0)</pre>
 generates an overall regression
                                                       summary(1mer5)
                                                       generates a regression for every diet
     Mixed Effect Model, Fixed intercept, Random slope
```



Questions?

```
synthetic <- data.frame(</pre>
  Person = LETTERS[1:4],
  Diet = rep(c(747, 0), each=2),
 Week0 = rnorm(4, mean=90, sd=15),
 Week1 = rep(0, 4),
 Week2 = rep(0, 4),
 Week3 = rep(0, 4)
b1 <- -5
sd1 <- 1
for(i in 1:2) {
  a <- synthetic$Week0[i]+b1+rnorm(1, mean=0, sd=sd1)</pre>
 b <- synthetic\$week0[i]+(2*b1)+rnorm(1, mean=0, sd=sd1)
  c <- synthetic$Week0[i]+(3*b1)+rnorm(1, mean=0, sd=sd1)</pre>
  synthetic$Week1[i]=a
  synthetic$Week2[i]=b
  synthetic$Week3[i]=c
b2 <- 0
sd2 <- 1
for(i in 3:4) {
  a <- synthetic$Week0[i]+b2+rnorm(1, mean=0, sd=sd2)</pre>
  b <- synthetic\\delta\eek0[i]+(2\delta\b2)+rnorm(1, mean=0, sd=sd2)
  c <- synthetic$Week0[i]+(3*b2)+rnorm(1, mean=0, sd=sd2)</pre>
  synthetic$Week1[i]=a
  synthetic$Week2[i]=b
  synthetic$Week3[i]=c
```



