ST 790, Homework 1 Solutions
Spring 2018

1. (a) Under these specifications,

$$Y_{ij} = \{(\beta_{0,1} + \beta_{1,1} t_{ij}) I(p_i = 1) + (\beta_{0,2} + \beta_{1,2} t_{ij}) I(p_i = 2) + (\beta_{0,3} + \beta_{1,3} t_{ij}) I(p_i = 3)\} + b_{0i} + e_{ij}, \quad (1)$$

where the indicator function $I(B) = 1$ if the event B is true and $= 0$ otherwise, so that it is immediate that

$$\text{var}(Y_{ij}|p_i) = D + \sigma^2, \quad \text{cov}(Y_{ij}, Y_{ij'}|p_i) = D,$$

and thus

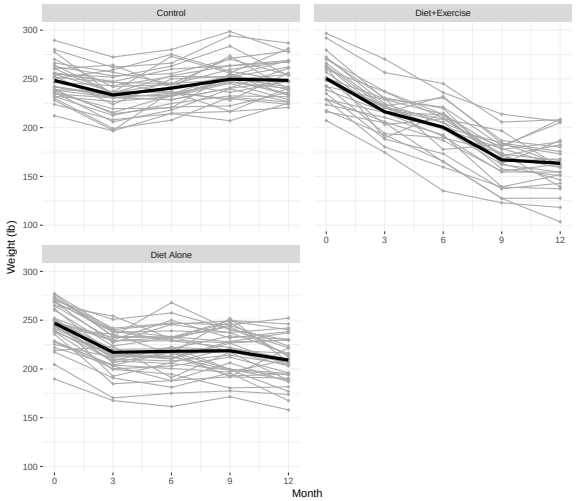
$$\text{corr}(Y_{ij}, Y_{ij'}|p_i) = \frac{D}{D + \sigma^2}.$$

Note that these values are the same for all weight loss programs. The correlation is the same for all pairs of time points, and the variance is constant across time, so it is clear that the covariance and correlation matrices for $\boldsymbol{Y}_i$ for each program have the compound symmetric form with the same variance at all time points. Moreover, these covariance and correlation matrices are the same for all programs.

(b) Comparing (1) to (3.1), both models involve an individual-specific random effect plus an independent within-individual deviation, so that the variance, covariance, and correlation are of the same form with D playing the role of σ_b^2 and σ^2 playing the role of σ_e^2. Thus, both models make the same assumption about the overall covariance and correlation structure of a data vector; namely, that it is compound symmetric with constant variance, and that the overall covariance structure is the same for all values of p_i (so for all three weight loss program groups).

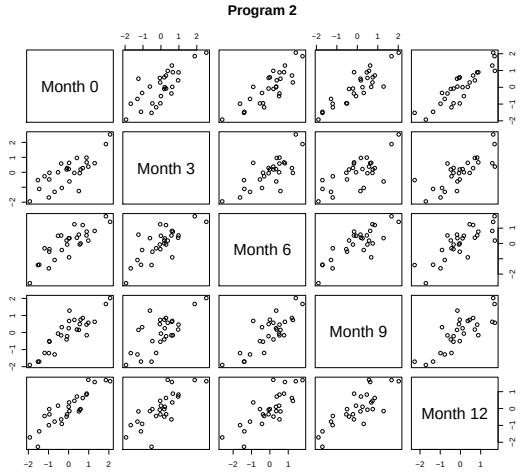
The major difference is how the population mean response profile is represented. In (1), the population means for each weight loss program at each time point lie on a straight line, where the intercepts and slopes are possibly different for each program. In (3.1), no relationship between the population means at each time point is assumed; each is modeled separately and is not constrained in any way to be related to any other mean.

(c) As always, the first thing you should do is create a spaghetti plot of the data; here, we superimpose the sample averages for each program.

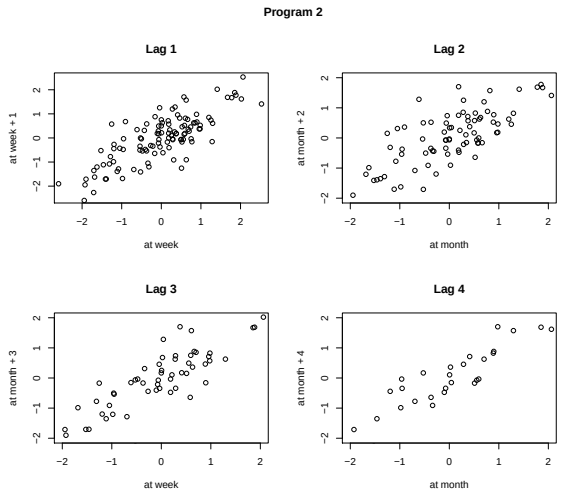


We comment on the nature of the population mean response in (d) below.

On the course website, there is an R program that produces the graphical and numerical analyses discussed in Section 2.5 of notes. The sample covariance and correlation matrices for each program are calculated, and the estimated standard deviations of weight at each time point for each program are also explicitly given. Eyeballing the variances on the diagonals of the covariance matrices and the accompanying SDs, the assumption of constant overall variance across time embodied in both of the models does not seem out of line, although there is some hint that variance/SD is smaller overall for the control group. Similarly, the visual impression from the sample correlation matrices is that they are all have an approximately compound symmetric form, although that seems a little less certain for the control group, for which the correlations are somewhat smaller overall. Scatterplot matrices reflect the a similar correlation among observations at any pair of time points; for illustration, here is the plot for program 2.



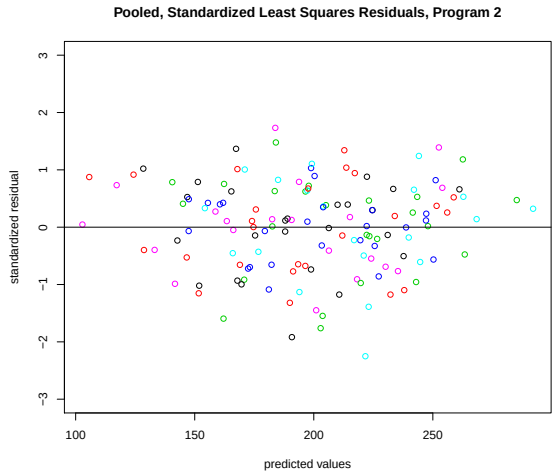
Because the time points here are equally spaced, it is reasonable to construct lag plots of centered and scaled responses and estimated autocorrelation functions under the assumption of stationarity (which of course is satisfied for compound symmetry). The lag plots tell a similar story of correlation begin similar between pairs 1, 2 3, or 4 lags (a lag begin 3 months) apart; here is the plot for program 2.



The accompanying estimated autocorrelation functions reflect this also; e.g., that for program 2 is

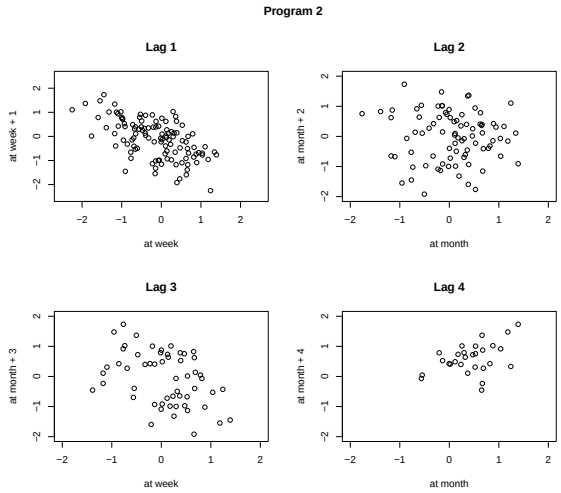
```
## > ac.two
## [1] 0.7884006 0.7844676 0.8307240 0.8911885
```

We can also investigate within-subject variance and correlation for further corroboration. Based on the individual-specific straight line model in (1), here is the plot of within-individual standardized residuals for program 2.



This and the analogous plots for the other two programs do not show any strong evidence of a departure from constant within-subject variance that is of similar magnitude for each program. In the attached program, estimates of the within-program based on pooled within-individual residuals are not terribly different; this is consistent with the assumption of the same within-individual variance across programs. Again, because the time points are equally spaced, it is reasonable to construct lag plots of standardized within-individual residuals and

estimated autocorrelation functions based on these measures. The estimated autocorrelation functions are all over the place! The accompanying lag plots are pretty unremarkable, though; here is the one for program 2.



With the exception of the lag 1 plot, which seems to show a negative pattern, the others seem to be more "cloud-like" and of course are based on smaller and smaller numbers of observations. It is hard to draw definitive conclusions, but we can take comfort in the fact that the overall pattern of correlation appears compound symmetric for all three programs.

Taking all of this together, there does not seem to be strong evidence against the assumption of an overall covariance structure that is compound symmetric with constant variance across time for each program. The further assumption that this covariance structure is the same for all programs is a little less certain, but the evidence against is not overwhelming.

Accordingly, of the models in Section 2.5, the unstructured and compound symmetric models with the same variance over time are the most plausible for representing the overall pattern of covariance for each program. Of course, the former is probably over-specified, as the correlations do seem mostly very similar for all pairs of time points. There does not seem to be any "damping out" of correlation over time for any of the programs, so the one- and higher-dependent and autoregressive models (recall the times are equally spaced) do not seem appropriate.

(d) Given the evidence supporting a possibly common overall covariance structure across all three weight loss programs that is compound symmetric with constant variance across time, it appears that the assumption about overall covariance in both models is plausible. However, there is a slight concern about a violation of this in that the sample correlations for program 1 seemed slightly less strong than for programs 2 and 3. So both models seem reasonable with this caveat.

From the spaghetti plots and sample means, there is definitely a systematic relationship between weight and time at both the individual and population levels in all three groups. As noted above, the model in (3.1) makes no assumption at all about any sort of systematic relationship between population means over time. So while it makes a plausible assumption about the population means (that they can be anything), it cannot take advantage of or represent a systematic pattern. The model in (a) assumes that the that the inherent

individual-specific trajectories are straight lines so that the overall population means are also straight lines, so embodies a specific assumption about the systematic relationship. From the plots and sample means, the assumption of the population means falling on a straight line as in the model in (a) does not seem unreasonable, although there is some slight suggestion of some possible curvature. As discussed in the notes, if such an assumption is justified, scientific questions can be formulated more directly than with model (3.1).

In summary, both models are reasonable, with the above caveats. Which model to choose depends on how one feels about the assumption of straight line relationships. One can be "safe" and use (3.1), but at the potential expense of making it more difficult to address questions of interest. One can adopt the model in (a) but at the expense ignoring possible curvature. As in any statistical modeling context, making these sorts of decisions should take account of both the evidence in the data and the science.

2. *Nonlinear models.*

(a) We wish to calculate

$$\begin{aligned}\mu(t) = E\{\mu_i(t)\} &= E\left[\frac{\beta_1}{1+\exp\{-(\beta_3+\beta_{2i}t)\}}\right] \\ &= \beta_1 E\left\{\frac{1}{1+e^{(A+b_it)}}\right\},\end{aligned}$$

where $A = \beta_3 + \beta_2 t$. Using the probit approximation (5), we can approximate this as

$$\beta_1 E\left\{\Phi\left(\frac{A}{c}+\frac{b_i t}{c}\right)\right\}.$$

We thus need to calculate this expectation. Writing $A_c = A/c = (\beta_3+\beta_2 t)/c$ for brevity,

$$\begin{aligned}&E\left\{\Phi\left(A_c+\frac{b_i t}{c}\right)\right\} \\ &= \frac{1}{(2\pi)^{1/2}D^{1/2}}\int_{-\infty}^{\infty}\Phi\left(A_c+\frac{b_i t}{c}\right)\, e^{-b_i/(2D)}\, db_i \\ &= \frac{1}{2\pi)^{1/2}D^{1/2}t/c}\int_{-\infty}^{\infty}\Phi\left(A_c+b\right)\, e^{-b/(2Dt^2/c^2)}\, db \\ &= \frac{1}{2\pi)^{1/2}D_c^{1/2}}\int_{-\infty}^{\infty}\Phi\left(A_c+b\right)\, e^{-b/(2D_c)}\, db, \quad D_c = Dt^2/c^2 \\ &= \frac{1}{D_c^{1/2}}\int_{-\infty}^{\infty}\Phi\left(A_c+b\right)\, \varphi(b/D_c^{1/2})\, db,\end{aligned}$$

where $\varphi(\cdot)$ is the standard normal probability density function.

This final integral can be found in various ways. One way is to look it up in an integral table. A good integral table will have

$$\int_{-\infty}^{\infty}\Phi(a+bx)\,\varphi(x)\,dx = \phi\left(\frac{a}{(1+b^2)^{1/2}}\right).$$

Thus, identifying $a = A_c$ and making a change of variables $x = b/D_c^{1/2}$, we get immediately that

$$\frac{1}{D_c^{1/2}}\int_{-\infty}^{\infty}\Phi\left(A_c+b\right)\, \varphi(b/D_c^{1/2})\, db = \Phi\left\{\frac{A_c}{(1+D_c)^{1/2}}\right\}. \tag{2}$$

Or you can do it yourself. Here are two ways to calculate this integral.

Easy way: Let $X \sim \mathcal{N}(0, D_c)$ and $Z \sim \mathcal{N}(0,1)$, where X and Z are independent. Then

$$\begin{aligned} P(X+Z<a) &= E\{I(X+Z<a)\} \\ &= E[E\{I(X+Z<a)|X\}] \\ &= E[P(X+Z<a|X)\} \\ &= \frac{1}{D_c^{1/2}} \int_{-\infty}^{\infty} P(Z<a-x|X=x)\varphi(x/D_c^{1/2})\,dx \\ &= \frac{1}{D_c^{1/2}} \int_{-\infty}^{\infty} \Phi(a-x)\varphi(x/D_c^{1/2})\,dx, \end{aligned}$$

where the last equality follows by the independence of X and Z. Upon the change of variables $b = -x$, this can be written as

$$\frac{1}{D_c^{1/2}} \int_{-\infty}^{\infty} \Phi(a+b)\varphi(b/D_c^{1/2})\,db,$$

which is the integral we seek with $a = A_c$. Now, because X and Z are independent and normal, we also know immediately that $X+Z \sim \mathcal{N}\{0,(1+D_c)^{1/2}\}$, from whence it follows that

$$P(X+Z<a) = P\left\{\frac{X+Z}{(1+D_c)^{1/2}} < \frac{a}{(1+D_c)^{1/2}}\right\} = \Phi\{a(1+D_c)^{-1/2}\}.$$

Putting this together, we obtain the result (2).

Thus, we find that the integral we are interested in is equal to $\Phi\{a(1+D_c)^{-1/2}\}$. Who said you would never use stuff you learned in ST 701/521?

Less easy, brute-force way: Letting $a = A_c$, the integral we seek can be written as

$$\frac{1}{(2\pi D_c)^{1/2}} \int_{-\infty}^{\infty} \left\{ \int_{-\infty}^{a+b} \frac{1}{2\pi} \exp\left(-\frac{u^2}{2}\right)\,du \right\} \exp\left(-\frac{b^2}{2D_c}\right)\,db.$$

Rewrite the inner integral to obtain

$$\frac{1}{(2\pi D_c)^{1/2}} \int_{-\infty}^{\infty} \left[\int_{-\infty}^{a} \frac{1}{(2\pi)^{1/2}} \exp\left\{-\frac{(u-b)^2}{2}\right\}\,du \right] \exp\left(-\frac{b^2}{2D_c}\right)\,db.$$

Switching the order of integration,

$$\frac{1}{(2\pi)^{1/2}} \int_{-\infty}^{a} \left(\int_{-\infty}^{\infty} \frac{1}{(2\pi D_c)^{1/2}} \exp\left[-\frac{1}{2D_c}\{D_c(u-b)^2+b^2\}\right]\,db \right) du.$$

By some algebra (complete the square), we can show that

$$D_c(u-b)^2 + b^2 = (1+D_c)\left(b - \frac{uD_c}{1+D_c}\right)^2 + \frac{D_c u^2}{1+D_c}.$$

Substituting this into the inner integral yields

$$\frac{1}{(2\pi)^{1/2}(1+D_c)^{-1/2}} \int_{-\infty}^{a} \left[\int_{-\infty}^{\infty} \frac{1}{(2\pi D_c)^{1/2}(1+D_c)^{-1/2}} \exp\left\{-\frac{\left(b-\frac{uD_c}{1+D_c}\right)^2}{2D_c(1+D_c)^{-1}}\right\}\,db \right] \exp\left\{-\frac{u^2}{2(1+D_c)}\right\}\,du.$$

Clearly, the inner integral is equal to 1, so that the expression reduces to

$$\frac{1}{(2\pi)^{1/2}(1+D_c)^{-1/2}}\int_{-\infty}^{a}\exp\left\{-\frac{u^2}{2(1+D_c)}\right\}du=\Phi\{a(1+D_c)^{-1/2}\}.$$

Thus, by these or still other arguments, we obtain (2).

Combining, we end up with the final result that

$$\begin{aligned}\mu(t)=E\{\mu_i(t)\}&=E\left[\frac{\beta_1}{1+\exp\{-(\beta_3+\beta_{2i}t)\}}\right]\\&\approx\beta_1 E\left\{\Phi\left(\frac{\beta_3+\beta_2 t+b_i t}{c}\right)\right\}\\&=\beta_1\Phi\left\{\frac{\beta_3+\beta_2 t}{c(1+D_c)^{1/2}}\right\}=\beta_1\Phi\left\{\frac{\beta_3+\beta_2 t}{(c^2+Dt^2)^{1/2}}\right\}\qquad(3)\\&=\beta_1\Phi\left\{\frac{\beta_2+\beta_3 t}{c(1+Dt^2/c^2)^{1/2}}\right\}\qquad(4)\end{aligned}$$

Using the probit approximation (5) again, the expression in (4) can be approximated again, leading to

$$\mu(t)\approx\frac{1}{1+\exp\{-(\beta_3+\beta_2 t)/(1+Dt^2/c^2)^{1/2}\}}.\qquad(5)$$

(b) Taking a linear Taylor series of $\mu_i(t)$ about $b_i=0$, we have

$$\begin{aligned}\mu_i(t)=\frac{\beta_1}{1+\exp\{-(\beta_3+\beta_2 t+b_i t)\}}&\approx\frac{\beta_1}{1+\exp\{-(\beta_3+\beta_2 t)\}}\\&\quad+\frac{\beta_1 t\exp\{-(\beta_3+\beta_2 t)\}}{[1+\exp\{-(\beta_3+\beta_2 t)\}]^2}b_i.\end{aligned}$$

Treating this linear approximation as exact, because $E(b_i)=0$, we obtain

$$\mu(t)=E\{\mu_i(t)\}\approx\frac{\beta_1}{1+\exp\{-(\beta_3+\beta_2 t)\}}\qquad(6)$$

which can be approximated as

$$\beta_1\Phi\left(\frac{\beta_3+\beta_2 t}{c}\right)$$

using the probit approximation.

(c) We can compare these two approximations on either the logistic or the approximate probit scales. On the logistic scale, comparing the (cruder) approximation (6) to the (more direct) approximation (5), we see that they are of the same logistic form. However, the argument of the exponential is

$$\frac{\beta_3+\beta_2 t}{(1+Dt^2/c^2)^{1/2}}$$

in the better approximation (5) versus

$$\beta_3+\beta_2 t$$

in the crude approximation (6). This suggests if we were to use the linear Taylor series as in (b) to approximate $\mu(t)$, the resulting estimators of β_2 and β_3 will not be estimating these

quantities but will instead be estimating quantities close to $\beta_2/(1 + Dt^2/c^2)^{1/2}$ and $\beta_3/(1 + Dt^2/c^2)^{1/2}$ Thus, they will yield overestimates of the true values of β_2 and β_3. Similarly, if we compare on the probit scales, the argument of the probit function for the better approximation (3) is

$$\frac{\beta_3 + \beta_2 t}{(c^2 + Dt^2)^{1/2}}$$

versus

$$\frac{\beta_3 + \beta_2 t}{c}.$$

Again, comparing these two expressions, because $Dt^2 > 0$, we expect the estimators for β_2 and β_3 using the crude Taylor series approximation to yield overestimates.

3. (a) This is entirely possible; the null hypothesis that the pattern of change is the same in all groups is just the hypothesis of parallelism. Here, then,

$$\mathcal{M} = \begin{pmatrix} \mu_{11} & \mu_{12} & \mu_{13} & \mu_{14} & \mu_{15} \\ \mu_{21} & \mu_{22} & \mu_{23} & \mu_{24} & \mu_{25} \\ \mu_{31} & \mu_{32} & \mu_{33} & \mu_{34} & \mu_{35} \end{pmatrix}.$$

If we take

$$\boldsymbol{U} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ -1 & 1 & 0 & 0 \\ 0 & -1 & 1 & 0 \\ 0 & 0 & -1 & 1 \\ 0 & 0 & 0 & -1 \end{pmatrix}$$

(or equivalently let $\boldsymbol{U}$ be another (5×4) matrix whose columns define appropriate contrasts of all pairs of means), and let

$$\boldsymbol{C} = \begin{pmatrix} 1 & -1 & 0 \\ 1 & 0 & -1 \end{pmatrix}$$

(or equivalently another (2×3) matrix whose rows define appropriate contrasts).

We can verify that this does indeed lead to the hypothesis of parallelism (that is, of no group by time interaction). With these definitions,

$$\mathcal{M}\boldsymbol{U} = \begin{pmatrix} \mu_{11} - \mu_{12} & \mu_{12} - \mu_{13} & \mu_{13} - \mu_{14} & \mu_{14} - \mu_{15} \\ \mu_{21} - \mu_{22} & \mu_{22} - \mu_{23} & \mu_{23} - \mu_{24} & \mu_{24} - \mu_{25} \\ \mu_{31} - \mu_{32} & \mu_{32} - \mu_{33} & \mu_{33} - \mu_{34} & \mu_{34} - \mu_{35} \end{pmatrix}.$$

This matrix contains differences of pairs of means at different time points for each group (rows). Premultiplying by $\boldsymbol{C}$ gives

$$\begin{pmatrix} (\mu_{11} - \mu_{12}) - (\mu_{21} - \mu_{22}) & (\mu_{12} - \mu_{13}) - (\mu_{22} - \mu_{23}) & \cdots & (\mu_{14} - \mu_{15}) - (\mu_{24} - \mu_{25}) \\ (\mu_{11} - \mu_{12}) - (\mu_{31} - \mu_{32}) & (\mu_{12} - \mu_{13}) - (\mu_{32} - \mu_{33}) & \cdots & (\mu_{14} - \mu_{15}) - (\mu_{34} - \mu_{35}) \end{pmatrix}$$

or, equivalently,

$$\begin{pmatrix} (\mu_{11} - \mu_{21}) - (\mu_{12} - \mu_{22}) & (\mu_{12} - \mu_{22}) - (\mu_{13} - \mu_{23}) & \cdots & (\mu_{14} - \mu_{24}) - (\mu_{15} - \mu_{25}) \\ (\mu_{11} - \mu_{31}) - (\mu_{21} - \mu_{32}) & (\mu_{12} - \mu_{32}) - (\mu_{13} - \mu_{33}) & \cdots & (\mu_{14} - \mu_{34}) - (\mu_{15} - \mu_{35}) \end{pmatrix}.$$

If this matrix is equal to zero, then it follows that the difference in mean response at each time point is the same for each group, so that the mean profiles are parallel, as desired.

(b) Your first thought may have been that this is not possible, as we have denigrated the repeated measures analysis of variance as not being able to represent things like rates of change. However, in the special case where the time points are equally spaced, as they are here, it is in fact possible to represent the hypothesis that the rate of change of mean response is constant for all groups.

When the time points are equally spaced, if, for each group $\ell = 1, 2, 3$,

$$\mu_{\ell 2} - \mu_{\ell 1} = \mu_{\ell 3} - \mu_{\ell 2} = \mu_{\ell 4} - \mu_{\ell 3} = \mu_{\ell 5} - \mu_{\ell 4} \tag{7}$$

or equivalently

$$\mu_{\ell 1} - \mu_{\ell 2} = \mu_{\ell 2} - \mu_{\ell 3} = \mu_{\ell 3} - \mu_{\ell 4} = \mu_{\ell 4} - \mu_{\ell 5},$$

then the $\mu_{\ell j}$ lie on a straight line, so that the rate of change of mean response is indeed constant. Thus, the null hypothesis that the rate of change is constant for all groups can be represented by (7) for $\ell = 1, 2, 3$.

It is possible to represent this null hypothesis as $\mathcal{M}\boldsymbol{U}$ as follows. Note that that (7) can be written as

$$\begin{aligned}
\mu_{\ell 2} - \mu_{\ell 1} - (\mu_{\ell 3} - \mu_{\ell 2}) &= 0 \\
\mu_{\ell 4} - \mu_{\ell 3} - (\mu_{\ell 3} - \mu_{\ell 2}) &= 0 \\
\mu_{\ell 5} - \mu_{\ell 4} - (\mu_{\ell 4} - \mu_{\ell 3}) &= 0
\end{aligned}$$

or equivalently

$$\begin{aligned}
\mu_{\ell 1} - 2\mu_{\ell 2} + \mu_{\ell 3} &= 0 \\
\mu_{\ell 2} - 2\mu_{\ell 3} + \mu_{\ell 4} &= 0 \\
\mu_{\ell 3} - 2\mu_{\ell 4} + \mu_{\ell 5} &= 0
\end{aligned}$$

for $\ell = 1, 2, 3$, which can be gotten by post-multiplying $\mathcal{M}$ by an appropriate $\boldsymbol{U}$ matrix. Such a $\boldsymbol{U}$ is

$$\boldsymbol{U} = \begin{pmatrix} 1 & 0 & 0 \\ -2 & 1 & 0 \\ 1 & -2 & 1 \\ 0 & 1 & -2 \\ 0 & 0 & 1 \end{pmatrix}.$$

Thus, with this $\boldsymbol{U}$, the null hypothesis can be written as $\mathcal{M}\boldsymbol{U} = \boldsymbol{0}$.

4. *Effectiveness of weight loss programs, continued.* The attached program shows a bunch of analyses using the methods in Chapter 3. You already investigated the covariance structure in Problem 1, which suggests that the model underlying the univariate repeated measures analysis of variance is reasonably appropriate for the data, with the caveat that the structure seemed slightly different for program 1. From those analyses, we don't know if the normality assumption is valid, of course, but hopefully it is not too unreasonable given the outcome is a weight measurement for which the normality assumption is often plausible. So we can have some faith that the analyses using the univariate methods are reasonably trustworthy, keeping in mind the possible mild violation of the common covariance structure assumption.

From the plot of the data given in the solution to Problem 1, the overall sample mean profiles suggest that the true underlying profiles may not be parallel, with that for program 2, the most rigorous program, showing a steeper decline than that for the less rigorous program, while that for the control program 1 appears to be relatively flat.

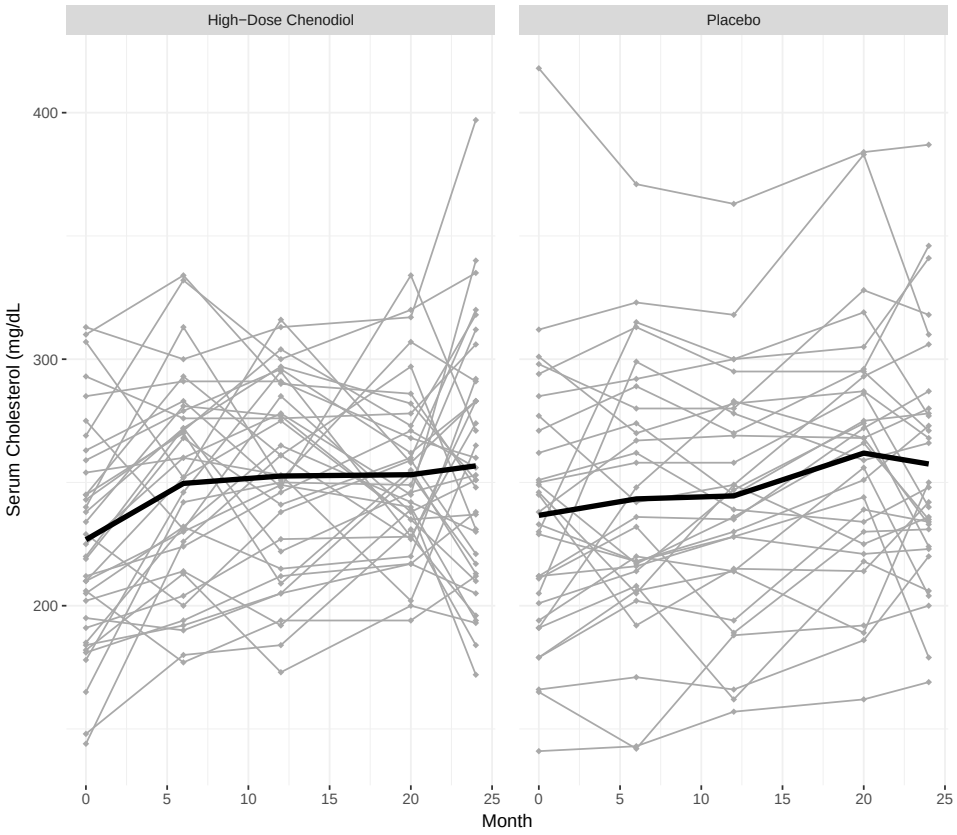
Mauchly's criterion yields a p-value of 0.09, which suggests that there is not overwhelming evidence against a Type H covariance structure, but if there really is not a common structure, this test will not be valid. Nonetheless, the evidence is overwhelming that the pattern of change is different across group, as the test of parallelism strongly rejects the null hypothesis. You should have stated formal hypotheses that address these issues. The specialized tests obtained from the orthogonal polynomial transformation that decompose the overall hypothesis of parallelism into linear, quadratic, cubic, and quartic components. The results for the linear component strongly suggest a difference across groups, while that for the quadratic component does not. As we discussed in class, the cubic and quartic component tests area harder to interpret, but overall seem to suggest some differences in more "local" curvature. These tests are valid even if compound symmetry does not hold, but they do require a common covariance structure across groups so are subject to the mild caveat noted above.

We can conclude from all of this that there seems to be strong evidence that the population mean profiles over the study period are not the same and in particular at least one of them follows a different long-term linear trend (steepness) than the others. It would be reasonable to conclude from this result and the visual evidence that at the very least the most rigorous weight loss program 2 is effective at lowering weight relative to control.

The multivariate analysis (if you did it) does not require compound symmetry but still requires a common pattern of covariance, so is subject to the same caveats. It leads to a similar conclusion that the population mean profiles are not all the same.

A statistical model that allows us to accommodate possibly different overall covariance structures would allow us to feel more confident about the interpretations here.

5. *Cholesterol Study.* Here is a plot of e the data. The individual-specific profiles are quite variable, but the overall sample mean profiles do not seem that much different between high-dose chenodiol and placebo.



The data are balanced but the observation times are not equally spaced. The sample variances for each group at each time point do not seem tremendously different, and they seem to stay relatively constant over time, which is good. Examination of the estimated correlation matrices in each group suggests that the correlation pattern might be approximately compound symmetric within the placebo group. However, that in the chenodiol group seems to exhibit some damping out of correlations as observations become farther apart in time. The sample size is not huge, so it is not out of the question that the estimated overall correlation matrix for this group could exhibit such a pattern if the true correlation structure really is compound symmetric.

So there is some concern that the structure of covariance and correlation is somewhat different in the two groups, which would violate a key assumption of the repeated measures analyses of variance. We thus should be cautious in interpreting the results, and you should have registered this concern in your report.

From the spaghetti plots, there are some unusual observations, including one individual in the chenodiol group whose cholesterol jumps up to nearly 400 mg/dL and another in the placebo group whose cholesterol was very high at baseline (time 0) and then dropped, but was still the highest of any subject over the course of the study. It is not clear to what extent the results are sensitive to these unusual observations.

Mauchley's criterion yields a p-value 0.01; as in the previous analysis, this test is only valid if the covariance structure is common across groups. Given the concern that this may not hold, we should not place too much stock in this test; however, it is not implausible that the result could be reflecting the fact that the correlation pattern seems to be a departure from

compound symmetry in the chenodiol group. Thus, we should interpret the results of the analyses with some skepticism, and you should have expressed this concern in your report.

The univariate hypothesis of parallelism is not rejected; even though the model assumptions likely do not hold, this result seems consistent with the visual evidence that there does not seem to be a difference in the pattern of change over time between the two groups. The test for a difference in linear trend yields a p-value close to 1, also suggesting little evidence for a difference in the general trend over time. The test for a difference in quadratic component, reflecting overall curvature, is suggestive of a difference, but given that we are not even confident that the required assumption of a common covariance structure for the validity of these analysis holds, it is not prudent to try to interpret this. The main effect of group also has a p-value close to 1, little evidence that, if the mean profiles are parallel, they are not coincident.

Overall, keeping in mind the caveat that these analyses are suspect because of the failure of the required assumptions to hold, it does not seem like there is much of interest going on here. There does not seem to be evidence of a different trend over time that would reflect an increase in mean cholesterol for chenodiol relative placebo.