

Biostatistics 200A
Problem Set 6

1. $RR = 2$; $P(A) = 0.2$; $p_{B|\bar{A}} = P(B|\bar{A}) = d$; $q_{B|\bar{A}} = P(\bar{B}|\bar{A}) = 1 - P(B|\bar{A}) = 1 - d$
- a. We define relative risk (RR) and odds ratio (OR) as follows:

$$RR = \frac{p_{B|A}}{p_{B|\bar{A}}}$$
$$\frac{p_{B|A}}{q_{B|A}}$$
$$\omega = \frac{p_{B|\bar{A}}}{q_{B|\bar{A}}}$$

If we take into consideration that $RR = 2$, we can observe that:

$$RR = \frac{p_{B|A}}{p_{B|\bar{A}}} = 2$$
$$\frac{p_{B|A}}{d} = 2$$
$$p_{B|A} = 2d$$

And therefore:

$$q_{B|A} = 1 - 2d$$

Thus, we can express the odds ratio in terms of d as follows:

$$\omega = \frac{2d/(1-2d)}{d/(1-d)} = \frac{2d(1-d)}{d(1-2d)} = \frac{2-2d}{1-2d}$$

And we can perform the following calculations:

$$\omega_{d=\frac{1}{10}} = \frac{2-2\left(\frac{1}{10}\right)}{1-2\left(\frac{1}{10}\right)} = \frac{2-0.2}{1-0.2} = \frac{1.8}{0.8}$$

$$\omega_{d=\frac{1}{100}} = \frac{2 - 2\left(\frac{1}{100}\right)}{1 - 2\left(\frac{1}{100}\right)} = \frac{2 - 0.02}{1 - 0.02} = \frac{1.98}{0.98}$$

$$\omega_{d=\frac{1}{1000}} = \frac{2 - 2\left(\frac{1}{1000}\right)}{1 - 2\left(\frac{1}{1000}\right)} = \frac{2 - 0.002}{1 - 0.002} = \frac{1.998}{0.998}$$

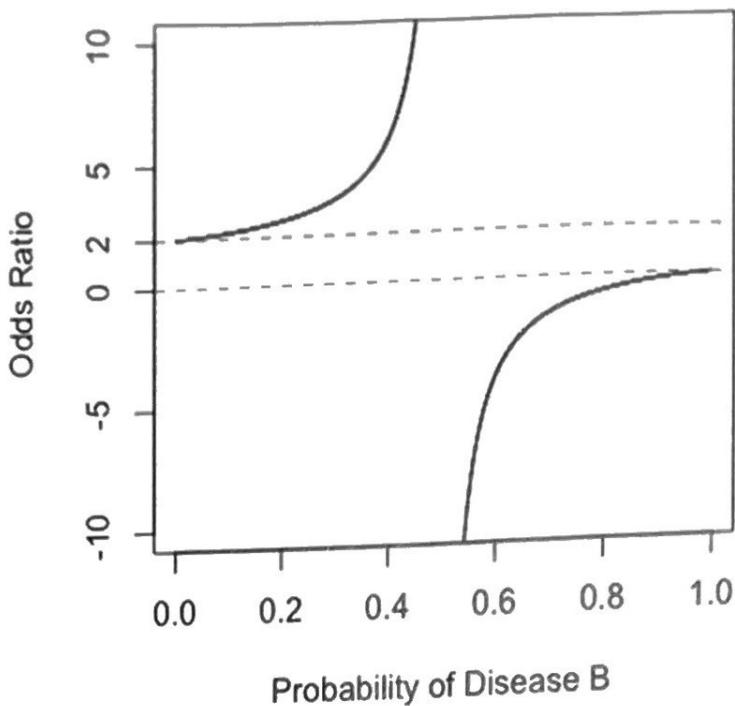
$$\omega_{d=\frac{1}{10000}} = \frac{2 - 2\left(\frac{1}{10000}\right)}{1 - 2\left(\frac{1}{10000}\right)} = \frac{2 - 0.0002}{1 - 0.0002} = \frac{1.9998}{0.9998}$$

$$\omega_{d=\frac{1}{100000}} = \frac{2 - 2d}{1 - 2d}$$

Below is a graph of odds ratio vs. the quantity d . By simple inspection of the plot, it is clear that when the probability of disease without exposure to risk factor A is sufficiently small, the odds ratio is an excellent estimator of the relative risk, which we know (in this case) to be 2. As d approaches 0.5, the odds ratio approaches infinity, and when d is greater than 0.5, the odds ratio approaches negative infinity from the right, and approaches 0 as d approaches 1. Therefore, the odds ratio is only a good estimator of relative risk when the probability of disease without exposure to risk factor is sufficiently small.

46
50

Odds Ratio vs. Probability of Disease B without Risk Factor A



- b. Referring back to our calculation of the odds ratio in part (a), all of the probabilities we invoked were those of B conditioned on A or not \bar{A} . Thus, altering the prevalence of exposure risk factor A in the population would not have an effect on the odds ratio, only the prevalence of the disease would. Since the relative risk was involved in our calculation of the odds ratio, and in particular since the odds ratio is an estimator of the relative risk when the disease prevalence is low, increasing or decreasing the relative risk would increase or decrease the odds ratio respectively. We should also note that if the relative risk is greater than 1, raising it would worsen the odds ratio approximation, while decreasing it would improve the odds ratio approximation. On the other hand, if relative risk were less than 1, raising it would improve the odds ratio approximation, while decreasing it would worsen the odds ratio approximation.

Good

2.

Matched-pair study results can be expressed in terms of a 2x2 contingency table as shown below. Because the study is matched-pair, the ideal test to perform is

McNemar's. The number of discordant pairs that we observed is less than 5, so it is reasonable to assume normality, and avoid performing an exact calculation.

Matched-pair results table:

b/c is small
better to do exact
test (binomial test)

	L	D	T
L	10	8	18
D	1	1	2
T	11	9	20

- 2

The R output is shown below. We have a $\chi^2 = 5.444$, and a p-value $p = 0.01963$, so at the $\alpha = 0.05$ confidence level, we can reject the null hypothesis that treatment A and treatment B are equally effective. We would expect that this is evidence in favor of the improved efficacy of simple mastectomy compared to radical mastectomy.

```
> mcnemar.test(cont_tab, correct=FALSE)
McNemar's Chi-squared test
data: cont_tab
McNemar's chi-squared = 5.4444, df = 1, p-value = 0.01963
```

3.

- a) The age-stratified data for the case-control study of disease X that we are analyzing is reproduced below for clarity:

Age 35-44 Stratum:

	H	L	T
Case	8	5	13
Control	62	164	126

T	70	169	139
---	----	-----	-----

Age 45-54 Stratum:

	H	L	T
Case	25	21	46
Control	29	138	167
T	54	159	213

Age 55-64 Stratum:

	H	L	T
Case	50	61	111
Control	27	208	235
T	77	269	346

An odds ratio for disease X and alcohol consumption (represented by A) is given by:

$$\hat{\omega} = \frac{\hat{p}_{X|H}/\hat{q}_{X|H}}{\hat{p}_{X|L}/\hat{q}_{X|L}} \cong \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}$$

Confidence intervals for odds ratios are constructed using a result of the approximation $\text{Var}(\ln[\hat{\omega}]) \cong \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}$, which gives us a 95% confidence interval defined by $\ln(\hat{\omega}) \pm z_{1-\alpha/2} \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$, or $\left(\hat{\omega} e^{-1.96\sqrt{\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}}}, \hat{\omega} e^{1.96\sqrt{\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}}} \right)$. And thus, we can calculate odds ratio point estimates and 95% confidence intervals for all three strata as follows:

$$\hat{\omega}_{35-44} = \frac{\binom{8}{70}}{\binom{5}{169}} / \frac{\binom{62}{70}}{\binom{164}{169}} = \frac{(8/62)}{\binom{5}{164}} = 4.232$$

$$95\% CI = \left(4.232 e^{-1.96\sqrt{\frac{1}{8}+\frac{1}{5}+\frac{1}{62}+\frac{1}{164}}}, 4.232 e^{1.96\sqrt{\frac{1}{8}+\frac{1}{5}+\frac{1}{62}+\frac{1}{164}}} \right) = (1.333, 13.433)$$

$$\hat{\omega}_{45-54} = \frac{\binom{25}{54}}{\binom{21}{159}} / \frac{\binom{29}{54}}{\binom{138}{159}} = \frac{(25/29)}{\binom{21}{138}} = 5.665$$

$$95\% CI = \left(5.665 e^{-1.96\sqrt{\frac{1}{25}+\frac{1}{21}+\frac{1}{29}+\frac{1}{138}}}, 5.665 e^{1.96\sqrt{\frac{1}{25}+\frac{1}{21}+\frac{1}{29}+\frac{1}{138}}} \right) = (2.799, 11.464)$$

$$\hat{\omega}_{55-64} = \frac{\binom{50}{77}}{\binom{61}{269}} / \frac{\binom{27}{77}}{\binom{208}{269}} = \frac{(50/27)}{\binom{61}{208}} = 6.315$$

$$95\% CI = \left(6.315e^{-1.96\sqrt{\frac{1}{50} + \frac{1}{61} + \frac{1}{27} + \frac{1}{208}}}, 6.315e^{1.96\sqrt{\frac{1}{50} + \frac{1}{61} + \frac{1}{27} + \frac{1}{208}}} \right) = (3.650, 10.925)$$

The calculations performed above are confirmed by the R output shown below:

```
> ## Problem 3 ##
> a <- c(8, 25, 50)
> b <- c(5, 21, 61)
> c <- c(62, 29, 27)
> d <- c(164, 138, 208)
> or <- c((a*d)/(b*c))
> CI_lo <- (or*exp(-1.96*sqrt((1/a)+(1/b)+(1/c)+(1/d))))
> CI_hi <- (or*exp(1.96*sqrt((1/a)+(1/b)+(1/c)+(1/d))))
> CI_lo
[1] 1.333474 2.799378 3.649598
> CI_hi
[1] 13.43259 11.46416 10.92533
```

Importantly, we can interpret these confidence intervals to mean that, with high likelihood, all three of the strata demonstrate an increased risk of disease when exposed to heavy alcohol consumption. We know this because none of the 95% confidence intervals contain the value 1, which would indicate no change in risk given exposure to the risk factor. We should note, however, that the effects of alcohol consumption could be drastically different in each group, given the width of the confidence intervals we calculated. The only similarity we can confidently assert, is that all three groups are at higher risk of disease given heavy alcohol consumption.

- b)
- As indicated in our response to part (a) above, we cannot make any statements about the similarity of the odds ratios found for each age stratum without additional analysis. Thus, we need to test for interaction (effect modification) using the hypotheses: $H_0: \omega_1 = \omega_2$ vs. $H_1: \omega_1 \neq \omega_2$. However, we are testing for effect modification across 3 tables, which means we also need to test the hypotheses: $H_0: \omega_1 = \omega_3$ vs. $H_1: \omega_1 \neq \omega_3$ and $H_0: \omega_2 = \omega_3$ vs. $H_1: \omega_2 \neq \omega_3$. These tests are performed below, and their results confirmed against R output:

$$H_0: \omega_1 = \omega_2 \text{ vs. } H_1: \omega_1 \neq \omega_2$$

$$\begin{aligned} T.S. &= \frac{\ln(\hat{\omega}_1) - \ln(\hat{\omega}_2) - 0}{\sqrt{Var(\ln(\hat{\omega}_1)) + Var(\ln(\hat{\omega}_2))}} \\ &= \frac{\ln(4.232) - \ln(5.665) - 0}{\sqrt{\frac{1}{8} + \frac{1}{5} + \frac{1}{62} + \frac{1}{164} + \frac{1}{25} + \frac{1}{21} + \frac{1}{29} + \frac{1}{138}}} = -0.422 \end{aligned}$$

$H_0: \omega_1 = \omega_3$ vs. $H_1: \omega_1 \neq \omega_3$

$$T.S. = \frac{\ln(\hat{\omega}_1) - \ln(\hat{\omega}_3) - 0}{\sqrt{Var(\ln(\hat{\omega}_1)) + Var(\ln(\hat{\omega}_3))}}$$

$$= \frac{\ln(4.232) - \ln(6.315) - 0}{\sqrt{\frac{1}{8} + \frac{1}{5} + \frac{1}{62} + \frac{1}{164} + \frac{1}{50} + \frac{1}{61} + \frac{1}{27} + \frac{1}{208}}} = -0.613$$

$H_0: \omega_2 = \omega_3$ vs. $H_1: \omega_2 \neq \omega_3$

$$T.S. = \frac{\ln(\hat{\omega}_2) - \ln(\hat{\omega}_3) - 0}{\sqrt{Var(\ln(\hat{\omega}_2)) + Var(\ln(\hat{\omega}_3))}}$$

$$= \frac{\ln(5.665) - \ln(6.315) - 0}{\sqrt{\frac{1}{25} + \frac{1}{21} + \frac{1}{29} + \frac{1}{138} + \frac{1}{50} + \frac{1}{61} + \frac{1}{27} + \frac{1}{208}}} = -0.238$$

```
> ## Problem 3 ##
> a <- c(8, 25, 50)
> b <- c(5, 21, 61)
> c <- c(62, 29, 27)
> d <- c(164, 138, 208)
> or <- c((a*d)/(b*c))
> ort1 <- c(log(or[1]), log(or[1]), log(or[2]))
> ort2 <- c(log(or[2]), log(or[3]), log(or[3]))
> tden <- c((1/a[1])+(1/b[1])+(1/c[1])+(1/d[1])+(1/a[2])+(1/b[2])+(1/c[2])+(1/d[2]),
+           (1/a[1])+(1/b[1])+(1/c[1])+(1/d[1])+(1/a[3])+(1/b[3])+(1/c[3])+(1/d[3]),
+           (1/a[2])+(1/b[2])+(1/c[2])+(1/d[2])+(1/a[3])+(1/b[3])+(1/c[3])+(1/d[3]))
> ts <- (ort1-ort2)/sqrt(tden)
> pval <- c(2*pnorm(ts, lower.tail=TRUE))
>
> ts
[1] -0.4223627 -0.6134126 -0.2382247
> pval
[1] 0.6727603 0.5396036 0.8117068
```

✓ Clearly, none of the p-values we generated suggest a significant difference between any of the odds ratios for any of the three contingency tables, and thus we can combine them and calculate a pooled estimate for the odds ratio, as well as a 95% confidence interval:

Use MH estimator when combining tables

- 2

```
> a_comb <- 0.25
> b_comb <- 0.75
> c_comb <- 0.3
> d_comb <- 0.7
> or_comb <- (a_comb*d_comb)/(b_comb*c_comb)
> CI_comb_lo <- (or_comb)*exp(-1.96*sqrt((1/a_comb)+(1/b_comb)+(1/c_comb)+(1/d_comb))))
> CI_comb_hi <- (or_comb)*exp(1.96*sqrt((1/a_comb)+(1/b_comb)+(1/c_comb)+(1/d_comb))))
> or_comb
[1] 4.12332
> CI_comb_lo
[1] 2.873039
> CI_comb_hi
[1] 5.917693
```

Thus, we have $\hat{\omega}_{combined} = 4.12$ with a 95% confidence interval of (2.873, 5.918). We can clearly see that the 95% confidence interval does not contain 1, and therefore, we can say that there is an association with heavy alcohol consumption and developing disease X among people 35-64 years of age.

c)

✓ It was certainly reasonable to stratify by age, because looking at the raw data it seems that age has an impact on a person's likelihood of developing disease X. By stratifying for age, we would be controlling for any confounding we might see on the basis of age. Because we analyzed the odds ratios and determined that they were not significantly across the three age groups, it was also reasonable to combine the data and analyze them as a whole. If we had not done a group-by-group analysis first, and had not tested the equality of the odds ratios, we would have been assuming no confounding was present, which there was presumably no way for us to know before we began data analysis.

4.

Pilot study summary:

Case — 0.25 lost parent ; 0.75 did not

Control — 0.1 lost parent ; 0.9 did not

New study info:

Case — p lost parent ; $1 - p$ did not

Control — 0.3 lost parent, 0.7 did not

a)

We can begin by observing an odds ratio for losing a parent before the age of 5 and "disturbed" status, using the data from the pilot study. In that case, $\omega_{pilot} = \frac{0.25 \times 0.9}{0.75 \times 0.1} = 3.0$. In order to estimate the sample size we need for 90% power at a confidence level of $\alpha = 0.05$, we can use the odds ratio from the pilot data as well as the fact that the proportion of controls with no loss of parent is 0.3 to determine that we would expect an odds ratio for the new study of $\frac{p \times 0.7}{(1-p) \times 0.3} = 3.0$, giving us:

$p = 0.562$ for the proportion of disturbed children who have lost a parent by the age of 5, and $1 - p = 0.438$ for the proportion of disturbed children who have not lost a

Use MH estimator when combining tables

- 2

```
> a_comb <- sum(a)
> b_comb <- sum(b)
> c_comb <- sum(c)
> d_comb <- sum(d)
> or_comb <- (a_comb*d_comb)/(b_comb*c_comb)
> CI_comb_lo <- (or_comb*exp(-1.96*sqrt((1/a_comb)+(1/b_comb)+(1/c_comb)+(1/d_comb)))) 
> CI_comb_hi <- (or_comb*exp(1.96*sqrt((1/a_comb)+(1/b_comb)+(1/c_comb)+(1/d_comb)))) 
> or_comb
[1] 4.12332
> CI_comb_lo
[1] 2.873039
> CI_comb_hi
[1] 5.917693
```

Thus, we have $\hat{\omega}_{combined} = 4.12$ with a 95% confidence interval of (2.873, 5.918). We can clearly see that the 95% confidence interval does not contain 1, and therefore, we can say that there is an association with heavy alcohol consumption and developing disease X among people 35-64 years of age.

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✓ It was certainly reasonable to stratify by age, because looking at the raw data it seems that age has an impact on a person's likelihood of developing disease X. By stratifying for age, we would be controlling for any confounding we might see on the basis of age. Because we analyzed the odds ratios and determined that they were not significantly across the three age groups, it was also reasonable to combine the data and analyze them as a whole. If we had not done a group-by-group analysis first, and had not tested the equality of the odds ratios, we would have been assuming no confounding was present, which there was presumably no way for us to know before we began data analysis.

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Pilot study summary:

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We can begin by observing an odds ratio for losing a parent before the age of 5 and "disturbed" status, using the data from the pilot study. In that case, $\omega_{pilot} = \frac{0.25 \times 0.9}{0.75 \times 0.1} = 3.0$. In order to estimate the sample size we need for 90% power at a confidence level of $\alpha = 0.05$, we can use the odds ratio from the pilot data as well as the fact that the proportion of controls with no loss of parent is 0.3 to determine that we would expect an odds ratio for the new study of $\frac{p \times 0.7}{(1-p) \times 0.3} = 3.0$, giving us:

$p = 0.562$ for the proportion of disturbed children who have lost a parent by the age of 5, and $1 - p = 0.438$ for the proportion of disturbed children who have not lost a

parent by the age of 5. Thus, if we intend to detect a difference between the proportion of disturbed children with parental loss and normal children with parental loss in the new study, we can conduct the following sample size calculation:

$$n_1 = n_2 = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta} \right)^2 (p_1 q_1 + p_2 q_2)}{(p_1 - p_2)^2}$$

$$= \frac{(1.96 + 1.282)^2 ((0.3)(0.7) + (0.562)(0.438))}{(0.3 - 0.562)^2} = 69.824$$

```
> (((qnorm(.975)+qnorm(.9))^2)*(0.3*.7+0.562*.438))/(0.262^2)
[1] 69.82437
```

✓ Thus, each group should have a sample size of 70, and our total sample size should be 140 subjects.

b)

If the proportion of normal children who had lost a parent were changed to 0.1, rather than 0.3, we would have the following calculation for the proportion of disturbed children who had lost parents in our new study, to yield an odds ratio of 3.0:
 $\frac{p \times 0.9}{(1-p) \times 0.1} = 3.0$. This yields $p = 0.25$. Thus, the sample size calculation would yield per group sample sizes of:

```
> (((qnorm(.975)+qnorm(.9))^2)*(0.1*.9+.25*.75))/(0.15^2)
[1] 129.5916
```

Conceptually, it also makes sense that since we have a decreased effect size, we would require an increased sample size. If the proportion were much larger, we would see an increased effect size, and therefore would need a smaller sample size.

5. If p_1 near 1, p_2 also near 1 so you would need a larger sample size.

a)

The following R code was used to simulate the study:

```

> a_chem_level <- rnorm(600, 12, 2)
> b_chem_level <- rnorm(600, 12, 2)
> t.test(a_chem_level, b_chem_level)

Welch Two Sample t-test

data: a_chem_level and b_chem_level
t = 0.39979, df = 1194.9, p-value = 0.6894
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
-0.1791342 0.2708226
sample estimates:
mean of x mean of y
12.03689 11.99104

```

The output corresponding with “mean of X” is actually the mean of the data generated for group A, while the output corresponding with “mean of Y” is actually the mean of the data generated for group B. Thus, the means for group A and B are 12.037 and 11.991, respectively. The two-sided p-value for the t-test is 0.6894, and thus the results of this study would not be considered statistically significant, and we would be unable to reject the null hypothesis that the blood chemical levels of drug A and drug B are equal. These results agree with those obtained by the pharmaceutical company. ✓

- b) Because we are performing 30 t-tests at a confidence level of $\alpha = 0.1$, we predict that 3 of the age group-specific t-tests would show significance, under the null hypothesis. Furthermore, the probability of finding at least one significance in our data generated from identical distributions can be calculated as follows:

$$P(\text{at least 1 significance}) = P(X \geq 1) = 1 - P(X = 0)$$

$$1 - P(X = 0) = \binom{30}{0} (0.9)^{30} (0.1)^0 = 1 - 0.042 = 0.958$$

The results of my simulation of the 30 age-specific t-tests are shown below:

```

> index <- vector()
> counter_low <- 1
> counter_high <- 20
> for (i in 1:30) {
+   if (t.test(a_chem_level[counter_low:counter_high],
+             b_chem_level[counter_low:counter_high])$p.value <= 0.1) {
+     index[i] <- 1
+   } else {
+     index[i] <- 0
+   }
+   counter_low <- counter_low+20
+   counter_high <- counter_high+20
+ }
> sig_num <- sum(index)
> sig_num
[1] 3
> index
[1] 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 0

```

It seems that significance was found in 3 of the age groups: 24-25, 74-75, and 76-77. This is exactly the number of “false positives” we would expect in 30 groups being tested at the of $\alpha = 0.1$ significance level. Although we have found significance in 3 of the groups, this does not suggest significance overall, and thus, we cannot reject the null hypothesis that the blood chemical levels for A and B across each age group is equal. Our results are similar to those obtained by the pharmaceutical company.

c)

As stated above, it is certainly not out of the question that two age groups were found to show significance based entirely on chance. Although the block randomization did help ensure that age was not responsible for any confounding effects on the data analysis, Analysis 1 is much more telling as is. If the drug company wanted to argue that significance is based on age, they would need to show that the age groups that were found to show significance were similar, and that such a finding was reproducible. We would need to see whether there are any trends in the p-values generated for each age group, to see if they appear randomly scattered or if they trend toward significance as you approach the age groups in question. It may be particularly effective, then, to create larger groups for better sample sizes and so that you could make statements about a larger demographic, especially if that demographic was defined by age. If the pooled data showed significance across an age range with biological significance (i.e. geriatrics), this result would be much more compelling. As is, I would not recommend accepting the drug company's logic, and would require further analysis or further testing to verify the results of this study. To reiterate, it is not at all unreasonable to suggest that the drug company's significant results were obtained purely by chance under the null hypothesis that the blood chemical levels of drug A and drug B are the same. Many further analyses would be required to suggest a significance trend across a meaningful age window that would require additional trials.

```

> index <- vector()
> counter_low <- 0
> counter_high <- 30
> for (i in 1:30) {
+   if (t.test(a$chem.level[counter_low:counter_high],
+             b$chem.level[counter_low:counter_high])$p.value <= 0.1) {index[i] <- 1} else {
+   }
+   counter_low <- counter_low+20
+   counter_high <- counter_high+20
+ }
> sig_num <- sum(index)
> sig_num
[1] 3
> index
[1] 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 0

```

It seems that significance was found in 3 of the age groups: 24-25, 74-75, and 76-77. This is exactly the number of “false positives” we would expect in 30 groups being tested at the of $\alpha = 0.1$ significance level. Although we have found significance in 3 of the groups, this does not suggest significance overall, and thus, we cannot reject the null hypothesis that the blood chemical levels for A and B across each age group is equal. Our results are similar to those obtained by the pharmaceutical company.

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As stated above, it is certainly not out of the question that two age groups were found to show significance based entirely on chance. Although the block randomization did help ensure that age was not responsible for any confounding effects on the data analysis, Analysis 1 is much more telling as is. If the drug company wanted to argue that significance is based on age, they would need to show that the age groups that were found to show significance were similar, and that such a finding was reproducible. We would need to see whether there are any trends in the p-values generated for each age group, to see if they appear randomly scattered or if they trend toward significance as you approach the age groups in question. It may be particularly effective, then, to create larger groups for better sample sizes and so that you could make statements about a larger demographic, especially if that demographic was defined by age. If the pooled data showed significance across an age range with biological significance (i.e. geriatrics), this result would be much more compelling. As is, I would not recommend accepting the drug company’s logic, and would require further analysis or further testing to verify the results of this study. To reiterate, it is not at all unreasonable to suggest that the drug company’s significant results were obtained purely by chance under the null hypothesis that the blood chemical levels of drug A and drug B are the same. Many further analyses would be required to suggest a significance trend across a meaningful age window that would require additional trials.

```
> index <- vector()
> counter_low <- 1
> counter_high <- 20
> for (i in 1:30) {
+
+   if (t.test(a_chem_level[counter_low:counter_high],
+             b_chem_level[counter_low:counter_high])$p.value <= 0.1) {index[i] <- 1} else {
+     index[i] <- 0
+   }
+ }
> counter_low <- counter_low+20
> counter_high <- counter_high+20
>
> sig_num <- sum(index)
> sig_num
[1] 3
> index
[1] 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 0
```

It seems that significance was found in 3 of the age groups: 24-25, 74-75, and 76-77. This is exactly the number of “false positives” we would expect in 30 groups being tested at the of $\alpha = 0.1$ significance level. Although we have found significance in 3 of the groups, this does not suggest significance overall, and thus, we cannot reject the null hypothesis that the blood chemical levels for A and B across each age group is equal. Our results are similar to those obtained by the pharmaceutical company.

c)

As stated above, it is certainly not out of the question that two age groups were found to show significance based entirely on chance. Although the block randomization did help ensure that age was not responsible for any confounding effects on the data analysis, Analysis 1 is much more telling as is. If the drug company wanted to argue that significance is based on age, they would need to show that the age groups that were found to show significance were similar, and that such a finding was reproducible. We would need to see whether there are any trends in the p-values generated for each age group, to see if they appear randomly scattered or if they trend toward significance as you approach the age groups in question. It may be particularly effective, then, to create larger groups for better sample sizes and so that you could make statements about a larger demographic, especially if that demographic was defined by age. If the pooled data showed significance across an age range with biological significance (i.e. geriatrics), this result would be much more compelling. As is, I would not recommend accepting the drug company’s logic, and would require further analysis or further testing to verify the results of this study. To reiterate, it is not at all unreasonable to suggest that the drug company’s significant results were obtained purely by chance under the null hypothesis that the blood chemical levels of drug A and drug B are the same. Many further analyses would be required to suggest a significance trend across a meaningful age window that would require additional trials.