STA305/1004 - Week 6

February 10, 2020

Class Outline

- Estimating the propensity score
- The balancing property of the propensity score
- Examples: Smoking Cessation, Maimonides' Rule
- Methods that use the propensity score
- Comparing more than 2 treatments

The propensity score in context

- The patient factors that were measured are age (x_1), sex (x_2), and health status before treatment (x_3).
- The propensity score can be estimated for each patient by fitting a logistic regression model with treatment as the dependent variable and x_1, x_2, x_3 as the predictor variables.

$$log\left(\frac{p_i}{1-p_i}\right) = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \beta_3 x_{i3},$$

where $p_i = P(T_i = 1)$.

The propensity score in context

- The predicted probabilities from the above equation are estimates of the propensity score for each patient.

$$\hat{p}_i = \frac{exp\left(\hat{\beta}_0 + \hat{\beta}_1 x_{i1} + \hat{\beta}_2 x_{i2} + \hat{\beta}_3 x_{i3}\right)}{1 + exp\left(\hat{\beta}_0 + \hat{\beta}_1 x_{i1} + \hat{\beta}_2 x_{i2} + \hat{\beta}_3 x_{i3}\right)}$$

The propensity score in Smoking Cessation Study

The propensity score for each subject in smoking and weight gain study can be estimated by fitting a logistic regression model.

```
prop.model <- glm(qsmk ~ as.factor(sex) + as.factor(race) +
                  age + as.factor(education.code) + smokeintensity +
                  smokeyrs  + as.factor(exercise) + as.factor(active) +
                  wt71, family = binomial(), data = nhefshwdat)

#Summary of propensity score model
summary(prop.model)
```

The propensity score in Smoking Cessation Study

	Estimate	Std. Error	z value
(Intercept)	-2.401228039	0.484016356	-4.9610473
as.factor(sex)1	-0.499080121	0.146530691	-3.4059767
as.factor(race)1	-0.778222994	0.207031619	-3.7589572
age	0.046207220	0.009889326	4.6724338
as.factor(education.code)2	-0.065716379	0.196122828	-0.3350777
as.factor(education.code)3	0.052634524	0.175523000	0.2998725
as.factor(education.code)4	0.108653058	0.269190883	0.4036283
as.factor(education.code)5	0.466164550	0.224105901	2.0801083
smokeintensity	-0.026527450	0.005664293	-4.6832762
smokeyrs	-0.028491730	0.010008629	-2.8467165
as.factor(exercise)1	0.359556747	0.178603430	2.0131570
as.factor(exercise)2	0.422771538	0.185656969	2.2771649
as.factor(active)1	0.044927909	0.131555137	0.3415139
as.factor(active)2	0.158150602	0.213435405	0.7409764
wt71	0.006099273	0.004368231	1.3962800

	Pr(>|z|)
(Intercept)	7.011411e-07
as.factor(sex)1	6.592780e-04
as.factor(race)1	1.706230e-04
age	2.976515e-06
as.factor(education.code)2	7.375665e-01
as.factor(education.code)3	7.642744e-01

How do we build a propensity score model?

- Usual tool is logistic regression model for the treatment allocation decision

– We therefore want to consider including any variables that have a relationship to the treatment decision (i.e. precede it in time, and are relevant)

– No information is included on the actual treatment received, or on the outcome(s).

Ten commandments of Propensity Model Development

1. Thou shalt value parsimony.
2. Thou shalt examine thy predictors for collinearity.
3. Thou shalt test all thy predictors for statistical significance.
4. Thou shalt have ten times as many predictors as subjects.
5. Thou shalt examine thy regression coefficients
6. Thou shalt perform bootstrap analyses to assess shrinkage.
7. Thou shalt perform regression diagnostics and examine residuals with care.
8. Thou shalt hold out a sample of thy data for cross-validation.
9. Thou shalt perform external validation on a new sample of data.
10. Thou shalt ignore commandments 1 through 9 and instead ensure that the model adequately balances covariates.

Propensity model development

1. Diagnostics for the successful prediction of probabilities and parameter estimates underlying those probabilities
2. Diagnostics for the successful design of observational studies based on estimated propensity scores.

In propensity score model development the second point is important, but the first is not important .

Propensity model development

- All covariates that subject matter experts (and subjects) judge important when selecting treatments.
- All covariates that relate to treatment and outcome, including any covariate that improves prediction (of exposure group).
- As much "signal" as possible.

Propensity score in smoking cessation study

The propensity score for each subject is $\hat{p}_i$ is the predicted probability of quitting smoking from the logistic regression model. The predicted probabilities are obtained using `predict()`.

```
#Propensity scores for each subject
p.qsmk.obs <- predict(prop.model, type = "response")
```

Propensity score in smoking cessation study

Subject	Quit Smoking	Estimated Propensity Score
1	0	0.12
2	0	0.16
3	0	0.16
4	0	0.31
5	0	0.32
6	0	0.17
7	0	0.24
8	0	0.26
9	0	0.30
10	0	0.29
11	1	0.26
12	0	0.19

- Subject 1's estimated probability of quitting smoking is 0.12 (so the estimated probability of not quitting smoking is 1- 0.12=0.82).
- Subject 11's estimated probability of quitting smoking (propensity score) is 0.26 (so the estimated probability of not quitting smoking is 1-.26=0.74).

Propensity score in smoking cessation study

```
p1 <- predict.glm(prop.model)[1]#predicted value for the first subject
p1
```

```
##         1
## -1.955973
```

```
exp(p1)/(1+exp(p1))
```

```
##         1
## 0.1239035
```

```
# use type="response" to get predicted
predict.glm(prop.model,type = "response")[1]
```

```
##         1
## 0.1239035
```

The balancing property of the propensity score

The balancing property of the propensity score says that treated ($T = 1$) and control ($T = 0$) subjects with the same propensity score $e(\mathbf{x})$ have the same distribution of the observed covariates, $\mathbf{x}$,

$$P(\mathbf{x}|T = 1, e(\mathbf{x})) = P(\mathbf{x}|T = 0, e(\mathbf{x}))$$

or

$$T \perp \mathbf{x} | e(\mathbf{x}).$$

This means that treatment is independent of the observed covariates conditional on the propensity score.

The balancing property of the propensity score

The balancing property says that if two units, i and j, are paired, one of whom is treated, $T_i + T_j = 1$, so that they have the same value of the propensity score $e(\mathbf{x}_i) = e(\mathbf{x}_j)$, then they may have different values of the observed covariate,

$$\mathbf{x}_i \neq \mathbf{x}_j,$$

but in this pair the specific value of the observed covariate will be unrelated to the treatment assignment since

$$P\left(\mathbf{x}|\, T = 1, e(\mathbf{x})\right) = P\left(\mathbf{x}|\, T = 0, e(\mathbf{x})\right)$$

The balancing property of the propensity score

The propensity scores for subject's 10 and 18 in the smoking cessation study are

	Quit Smoking	Estimated Propensity Score
10	0	0.2941244
18	1	0.3197956

The difference between the two subject's propensity scores are 0.32-0.29=0.03. This could be set as a "caliper" or "tolerance" for what are considered equal propensity scores.

The covariates for each subject are

	age	sex	race	edu	smkint	smkyrs	exer	active	wt1971	qsmk
10	43	0	0	2	20	25	2	1	62.26	0
18	48	1	0	3	2	30	1	1	62.03	1

The balancing property of the propensity score

- If many pairs are formed way then the the distribution of the observed covariates will look about the same in the treated and control groups.
- Individuals in matched pairs will typically have different values of x.
- It is difficult to match on 9 covariates at once, it is easy to match on one covariate, the propensity score $e(\mathbf{x})$, and matching on $e(\mathbf{x})$ will tend to balance all 9 covariates.

How can the degree of balance in the covariate distributions between treated and control units be assessed?

The balancing property of the propensity score

Q: What is the difference in using the propensity score to form two groups versus using randomization to form groups?

Assessing balance

- The difference in average covariate values by treatment status, scaled by their sample standard deviation. This provides a scale-free way to assess the differences.
- As a rule-of-thumb, when treatment groups have important covariates that are more than one-quarter or one-half of a standard deviation apart, simple regression methods are unreliable for removing biases associated with differences in covariates (Imbens and Rubin (2015)).

Assessing balance

If $\bar{x}_t, s_t^2$ are the mean and variance of a covariate in the treated group and $\bar{x}_c, s_c^2$ are the mean and variance of a covariate in the control group then the pooled variance is

$$\sqrt{\frac{s_t^2 + s_c^2}{2}}.$$

The absolute pooled standardized difference is,

$$\frac{100 \times |\bar{x}_t - \bar{x}_c|}{\sqrt{\frac{s_t^2 + s_c^2}{2}}}.$$

Assessing balance

The absolute pooled standardized difference between the groups can be calculated for all the covariates using the function `MatchBalance` in the library `Matching`.

```
library(Matching)
mb <- MatchBalance(qsmk ~ as.factor(sex) + as.factor(race) +
                       age + as.factor(education.code) +
                       smokeintensity + smokeyrs  +
                       as.factor(exercise) +
                       as.factor(active) + wt71, data=nhefshwdat,nboots=1
```

If the absolute value of the standardized mean difference is greater than 10% then this indicates a serious imbalance. For example, sex has an absolute standardized mean difference of $|-16.022| = 16.022$ indicating serious imbalance between the groups in males and females.

Assessing balance in the smoking cessation study

Output from `MatchBalance()`.

```
***** (V3) age *****
before matching:
mean treatment........ 46.174
mean control.......... 42.788
std mean diff......... 27.714

NB: some output is omitted ...
```

If the absolute value of the standardized mean difference is greater than 10% then this indicates a serious imbalance. Age has an absolute standardized mean difference of 27.714 indicating serious imbalance between the groups in age.

Assessing balance in the smoking cessation study

```
***** (V2) as.factor(race)1 *****
before matching:
mean treatment........ 0.08933
mean control.......... 0.14617
std mean diff......... -19.905

mean raw eQQ diff..... 0.057072
med  raw eQQ diff..... 0
max  raw eQQ diff..... 1

mean eCDF diff........ 0.028422
med  eCDF diff........ 0.028422
max  eCDF diff........ 0.056844

var ratio (Tr/Co)..... 0.65287
T-test p-value........ 0.0012863
```

Assessing Balance in the smoking cessation study

```
***** (V14) wt71 *****
before matching:
mean treatment........ 72.355
mean control.......... 70.303
std mean diff......... 13.13

mean raw eQQ diff..... 2.1872
med  raw eQQ diff..... 2.04
max  raw eQQ diff..... 14.75

mean eCDF diff........ 0.032352
med  eCDF diff........ 0.032386
max  eCDF diff........ 0.07

var ratio (Tr/Co)..... 1.0606
T-test p-value........ 0.022421
KS Bootstrap p-value.. 0.1
KS Naive p-value...... 0.10646
KS Statistic.......... 0.07
```

Propensity scores and ignorable treatment assignment

Assume that the treatment assignment T is strongly ignorable. This means that

$$P(T|Y(0), Y(1), \mathbf{x}) = P(T|\mathbf{x}),$$

or

$$T \perp Y(0), Y(1)|\mathbf{x}.$$

It may be difficult to find a treated and control unit that are closely matched for every one of the many covariates in x, but it is easy to match on one variable, the propensity score, $e(\mathbf{x})$, and doing that will create treated and control groups that have similar distributions for all the covariates.

Propensity scores and ignorable treatment assignment

Ignorable treatment assignment implies that

$$P(T|Y(0), Y(1), e(\mathbf{x})) = P(T|e(\mathbf{x})),$$

or

$$T \perp Y(0), Y(1)|e(\mathbf{x}).$$

This means that the scalar propensity score $e(\mathbf{x})$ may be used in place of the many covariates in $\mathbf{x}$.

Propensity scores and ignorable treatment assignment

- The propensity score can be used in place of many covariates.
- If treatment assignment is strongly ignorable then propensity score methods will produce unbiased results of the treatment effects.
- In the smoking cessation study what does it mean for treatment assignment to be ignorable?
- The potential outcomes for weight gain in the smoking cessation (treated) and smoking (control) groups are independent conditional on the propensity score.
- The treatment assignment mechanism has been reconstructed using the propensity score.

Propensity scores and ignorable treatment assignment

- Suppose a critic came along and claimed that the study did not measure an important covariate (e.g., spouse is a smoker) so the study is in no position to claim that the smoking cessation group and the smoking groups are comparable.
- This criticism could be dismissed in a randomized experiment — randomization does tend to balance unobserved covariates — but the criticism cannot be dismissed in an observational study.
- This difference in the unobserved covariate, the critic continues, is the real reason outcomes differ in the treated and control groups: it is not an effect caused by the treatment, but rather a failure on the part of the investigators to measure and control imbalances in the unobserved covariate.
- The sensitivity of an observational study to bias from an unmeasured covariate is the magnitude of the departure from the model that would need to be present to materially alter the study's conclusions.
- There are statistical methods to measure how sensitive an observational study is to this type of bias.

Using the propensity score to reduce bias

The three most common techniques that use the propensity score are

1. matching,
2. stratification (also called subclassification)
3. regression adjustment.

- Each of these techniques is a way to make an adjustment for covariates prior to (matching and stratification) or while (stratification and regression adjustment) calculating the treatment effect.
- With all three techniques, the propensity score is calculated the same way, but once it is estimated it is applied differently.

Class Outline

- Example: Maimonides Rule
- Methods that use the propensity score

Maimonides' Rule

- Educators are very interested in studying the effect of class size on learning.
- Does smaller class size cause students to achieve higher math and verbal scores?
- Angrist and Lavy (1999) published an unusual study of the effects of class size on academic achievement.
- Causal effects of class size on pupil achievement is difficult to measure. The twelfth century Rabbinic scholar Maimonides interpreted the Talmud's discussion of class size as:
- "Twenty-five children may be put in charge of one teacher. If the number in the class exceeds twenty-five but is not more than forty, he should have an assistant to help with instruction. If there are more than forty, two teachers must be appointed."

Maimonides' Rule

- Since 1969, the rule has been used to determine class size in Israeli public schools.
- Class size is usually determined by other factors such as wealth of a community, special needs of students, etc.
- If adherence to Maimonides' rule were perfectly rigid, then what would separate a school with a single class of size 40 from the same school with two classes whose average size is 20.5 is the enrollment of a single student.

Number of children in grade 5	40	80	120
Class size with one extra student	20.5	27	30.25

Maimonides' Rule

- Angrist and Lavy matched schools where the number of grade 5 students are 31-40 to schools where the number of grade 5 students are 41-50.
- 86 matched pairs of two schools were formed, matching to minimize to total absolute difference in percentage disadvantaged.
- It's plausible that whether or not a few more students enrol in the fifth grade is a haphazard event.
- This is an example of natural experiment where students were haphazardly (randomly) assigned to small or large grade 5 classes.
- It was haphazard because it depended only on the number of grade 5 children at a school.

Maimonides' Rule

From Rosenbaum, 2010, pg.9

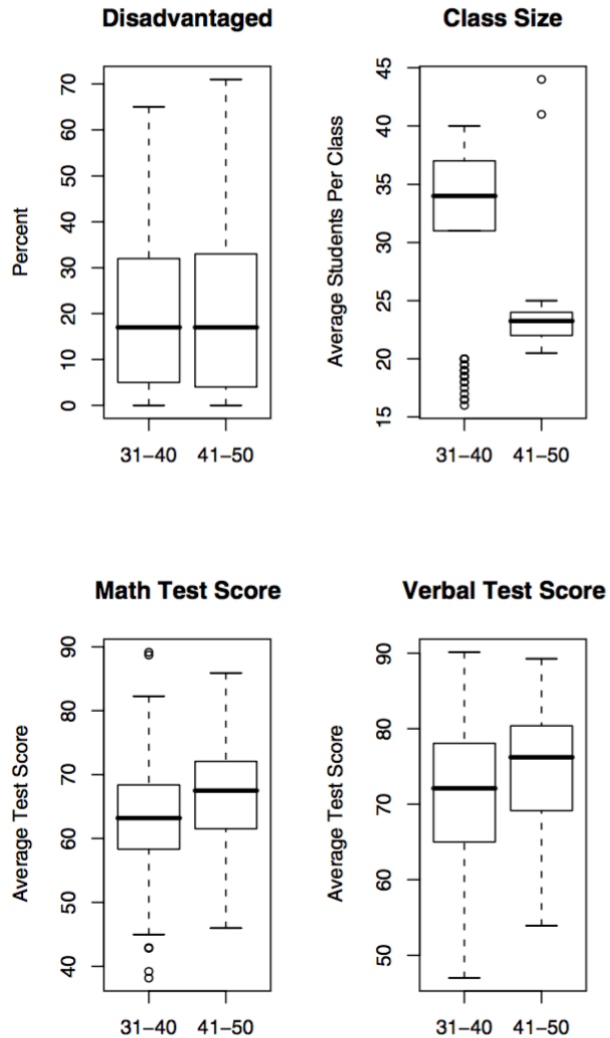


Fig. 1.1 Eighty-six pairs of two Israeli schools, one with between 31 and 40 students in the fifth grade, the other with between 41 and 50 students in the fifth grade, matched for percentage of students in the school classified as disadvantaged. The figure shows that the percentage of disadvantaged students is balanced, that imperfect adherence to Maimonides' rule has yielded substantially different average class sizes, and test scores were higher in the group of schools with predominantly smaller class sizes.

Figure

Propensity score matching

- In the Maimonides rule study assignment to a small/large was haphazard/random.
- If there is no opportunity to take advantge of this type of treatment assignment then we can calculate the propensity score and use this to match.
- For each unit we have a propensity score.
- Randomly select a treated subject.
- Match to a control subject with closest propensity score (within some limit or "calipers").
- Eliminate both units from the pool of subjects until there is no acceptable match.
- It's not always possible to match every unit treated to a unit that is not treated.

Propensity score matching

```
#prop.model <- glm(qsmk ~ as.factor(sex) + as.factor(race) +
 #                    age + as.factor(education.code) +
  #                   smokeintensity + smokeyrs  +
   #                  as.factor(exercise) + as.factor(active) +
    #                 wt71, family = binomial(),
     #                data = nhefshwdat)
X <- prop.model$fitted;Y <- nhefshwdat$wt82_71; Tr <- nhefshwdat$qsmk
library(Matching)
rr <- Match(Y=Y,Tr=Tr,X=X,M=1); summary(rr)
```

```
Estimate...  2.9342
AI SE......  0.5838
T-stat.....  5.026
p.val......  5.0087e-07

Original number of observations..............  1566
Original number of treated obs...............  403
Matched number of observations...............  403
Matched number of observations  (unweighted).  1009
```

Propensity score matching

After matching on covariates the treatment effect (difference in weight gain between the group that stopped smoking and the group that did not stop smoking) is 2.93 with a p-value of 0 (5.0087e-07) and 95% confidence interval (1.84, 4.02).

Propensity score matching -check covariate balance

Now, let's check covariate balance.

```
MatchBalance(qsmk ~ as.factor(sex) + as.factor(race) +
                    age + as.factor(education.code) +
                    smokeintensity + smokeyrs  +
                    as.factor(exercise) +
                    as.factor(active) + wt71, data=nhefshwdat,
                    match.out=rr,nboots=10)
```

Propensity score matching -check covariate balance

```
***** (V1) as.factor(sex)1 *****
                        Before Matching       After Matching
mean treatment........    0.45409             0.45409
mean control..........    0.53396             0.45331
std mean diff.........    -16.022             0.15703

NB: some output ommitted

***** (V3) age *****
                        Before Matching       After Matching
mean treatment........     46.174              46.174
mean control..........     42.788              46.595
std mean diff.........     27.714             -3.4504

NB: some output ommitted
```

Sex has an absolute standardized difference of 16 before matching and 0.16 after matching, and the absolute standardized difference of age has shifted from 27.71 to -3.45.

Propensity score matching -check covariate balance

How does this compare to not adjusting for imbalance?

```
#Unadjusted t-test
t.test(nhefshwdat$wt82_71[as.factor(nhefshwdat$qsmk)==1],
       nhefshwdat$wt82_71[as.factor(nhefshwdat$qsmk)==0],
       var.equal=T)
```

```
    Two Sample t-test

data:  nhefshwdat$wt82_71[as.factor(nhefshwdat$qsmk) == 1] and nhefshwd
t = 5.6322, df = 1564, p-value = 2.106e-08
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 1.655796 3.425367
sample estimates:
mean of x mean of y
 4.525079  1.984498
```

The unadjusted treatment effect is 2.54 with a p-value of 0. So, both analyses lead to the same conclusion that stopping to smoke leads to a significant weight gain. Although the weight gain in the matched propensity score analysis is 0.39Kg higher.

Propensity score subclassification/stratification

Propensity scores permit subclassification on multiple covariates simultaneously. One advantage of this method is that the whole sample is used and not just matched sets.

Cochran (1968) showed that creating five strata removes 90 per cent of the bias due to the stratifying variable or covariate.

Rosenbaum and Rubin holds for stratification based on the propensity score. Stratification on the propensity score balances all covariates that are used to estimate the propensity score, and often five strata based on the propensity score will remove over 90 per cent of the bias in each of these covariates.

Stratification

The following data were selected from data supplied to the U. S. Surgeon General's Committee from three of the studies in which comparisons of the death rates of men with different smoking habits were made (Cochran, 1968).

The table shows the unadjusted death rates per 1,000 person-years.

Smoking group	Canadian	British	U.S.
Non-smokers	20.2	11.3	13.5
Cigarettes only	20.5	14.1	13.5
Cigars, pipes	35.5	20.7	17.4

Conclusion: urge the cigar and pipe smokers to give up smoking and if they lack the strength of will to do so, they should switch to cigarettes.

Stratification

- Are there other variables in which the three groups of smokers may differ, that (i) are related to the probability of dying; and (ii) are clearly not themselves affected by smoking habits?
- The regression of probability of dying on age for men over 40 is a concave upwards curve, the slope rising more and more steeply as age advances. The mean ages for each group in the previous table are as follows.

Smoking group	Canadian	British	U.S.
Non-smokers	54.9	49.1	57.0
Cigarettes only	50.5	49.8	53.2
Cigars, pipes	65.9	55.7	59.7

Stratification

- The table shows the adjusted death rates obtained when the age distributions were divided into 9 subclasses.
- The results are similar for different numbers of subclasses.

Smoking group	Canadian	British	U.S.
Non-smokers	20.2	11.3	13.5
Cigarettes only	29.5	14.8	21.2
Cigars, pipes	19.8	11.0	13.7

Compare to the unadjusted death rates

Smoking group	Canadian	British	U.S.
Non-smokers	20.2	11.3	13.5
Cigarettes only	20.5	14.1	13.5
Cigars, pipes	35.5	20.7	17.4

Cochran (1968) showed that creating 5 or more strata removes 90% of the bias due to the stratifying variable.

Propensity score subclassification/stratification

```
prop.model <- glm(qsmk ~ as.factor(sex) + as.factor(race) +
                    age + as.factor(education.code) +
                    smokeintensity + smokeyrs  +
                    as.factor(exercise) + as.factor(active) +
                    wt71, family = binomial(),
                    data = nhefshwdat)
p.qsmk.obs <- predict(prop.model, type = "response")
strat <- quantile(p.qsmk.obs,probs = c(.2,.4,.6,.8))
strat1 <- p.qsmk.obs<=strat[1]
propmodel1 <- glm(wt82_71[strat1]~qsmk[strat1],data=nhefshwdat)
summary(propmodel1)
strat2 <- p.qsmk.obs > strat[1] & p.qsmk.obs <= strat[2]
propmodel2 <- glm(wt82_71[strat2]~qsmk[strat2], data=nhefshwdat)
summary(propmodel2)
strat3 <- p.qsmk.obs > strat[2] & p.qsmk.obs <= strat[3]
propmodel3 <- glm(wt82_71[strat3]~qsmk[strat3], data=nhefshwdat)
summary(propmodel3)
strat4 <- p.qsmk.obs > strat[3] & p.qsmk.obs <= strat[4]
propmodel4 <- glm(wt82_71[strat4]~qsmk[strat4], data=nhefshwdat)
summary(propmodel4)
strat5 <- p.qsmk.obs > strat[4]
propmodel5 <- glm(wt82_71[strat5]~qsmk[strat5], data=nhefshwdat)
summary(propmodel5)
```

Propensity score subclassification/stratification

```
             Estimate Std. Error  t value     Pr(>|t|)
(Intercept)  3.582883  0.4463651 8.026799 2.055049e-14
qsmk[strat1] 1.571867  1.2204794 1.287909 1.987319e-01
```

```
             Estimate Std. Error  t value     Pr(>|t|)
(Intercept)  2.700017  0.4466046 6.045654 4.258361e-09
qsmk[strat2] 5.054241  1.0286540 4.913451 1.449627e-06
```

```
             Estimate Std. Error  t value     Pr(>|t|)
(Intercept)  2.121351  0.5384292 3.939888 0.0001007005
qsmk[strat3] 3.726930  1.0519470 3.542888 0.0004564504
```

```
              Estimate Std. Error  t value     Pr(>|t|)
(Intercept)  0.9552357  0.5130865 1.861744 6.358234e-02
qsmk[strat4] 3.8711676  0.9463872 4.090469 5.488916e-05
```

```
               Estimate Std. Error    t value   Pr(>|t|)
(Intercept)  -0.2892809  0.5878199 -0.4921251 0.62297810
qsmk[strat5]  2.0550465  0.9192030  2.2356829 0.02608187
```

Propensity score subclassification/stratification

In summary the 5 quintiles produced treatment effects

Estimate (se)	P-value	PS Quintile
1.57 (1.22)	0.199	1
5.05 (1.03)	0.00	2
3.73 (1.05)	0.00	3
3.87 (0.95)	0.00	4
2.06 (0.92)	0.03	5

- The overall treatment effect is 3.26, which can be obtained by averaging the estimates within each stratum.
- This is a larger estimate compared to the treatment effect obtained by matching.
- The treatment effect and can also be estimated by fitting a linear regression model for the change in weight on the treatment variable and the quintiles of the estimated propensity score.

Propensity score subclassification/stratification

```
attach(nhefshwdat)
#create a variable to describe subclass to include in the model
stratvar <- numeric(length(qsmk))
for (i in 1:length(qsmk))
  {
if (strat1[i]==T) {stratvar[i] <- 1}
else
  if (strat2[i]==T) {stratvar[i] <- 2}
else
  if (strat3[i]==T) {stratvar[i] <- 3}
else
  if (strat4[i]==T) {stratvar[i] <- 4}
else stratvar[i] <- 5
}
stratmodel <- glm(wt82_71~qsmk+as.factor(stratvar),data=nhefshwdat)
summary(stratmodel)$coef
```

Propensity score matching

```
#prop.model <- glm(qsmk ~ as.factor(sex) + as.factor(race) +
 #                    age + as.factor(education.code) +
  #                   smokeintensity + smokeyrs  +
   #                  as.factor(exercise) + as.factor(active) +
    #                 wt71, family = binomial(),
     #                data = nhefshwdat)
X <- prop.model$fitted;Y <- nhefshwdat$wt82_71; Tr <- nhefshwdat$qsmk
library(Matching)
rr <- Match(Y=Y,Tr=Tr,X=X,M=1); summary(rr)
```

```
Estimate...  2.9342
AI SE......  0.5838
T-stat.....  5.026
p.val......  5.0087e-07

Original number of observations..............  1566
Original number of treated obs...............  403
Matched number of observations...............  403
Matched number of observations  (unweighted).  1009
```

Propensity score subclassification/stratification

```
                          Estimate Std. Error    t value     Pr(>|t|)
(Intercept)              3.3564796  0.4373149  7.6752008 2.894022e-14
qsmk                     3.2645028  0.4542610  7.1864036 1.027063e-12
as.factor(stratvar)2    -0.3191003  0.6134512 -0.5201723 6.030173e-01
as.factor(stratvar)3    -1.1139815  0.6157083 -1.8092683 7.060174e-02
as.factor(stratvar)4    -2.2229271  0.6172504 -3.6013378 3.265030e-04
as.factor(stratvar)5    -4.1403625  0.6255644 -6.6186033 4.971650e-11

                             2.5 %      97.5 %
(Intercept)              2.499358  4.21360105
qsmk                     2.374168  4.15483802
as.factor(stratvar)2    -1.521443  0.88324196
as.factor(stratvar)3    -2.320748  0.09278456
as.factor(stratvar)4    -3.432716 -1.01313860
as.factor(stratvar)5    -5.366446 -2.91427883
```

The linear regression yields the same treatment effect as averaging the estimates, but also provides an estimate of standard error, p-value, and confidence interval for the treatment effect.

Propensity score subclassification/stratification

We can investigate covariate balance within subclasses. In practice this should occur prior to looking at the outcome data. The number of subjects and average propensity score (shown in brackets) within each treatment group by subclass is shown in the table below.

Subclass	Smoking Cessation	No smoking cessation
1	42 (0.14)	272 (0.12)
2	59 (0.2)	254 (0.19)
3	82 (0.24)	231 (0.24)
4	92 (0.31)	221 (0.3)
5	128 (0.43)	185 (0.41)

For example, the percentage of males in each subclass are:

Subclass	Smoking Cessation	No Smoking Cessation
1	28.57%	22.79%
2	44.07%	43.31%
3	54.88%	46.32%
4	55.43%	59.73%
5	67.19%	70.81%

Multivariate adjustment using the propensity score

- Another method for using the propensity score to adjust for bias is to use the propensity score itself as a predictor along with the treatment indicator.
- The treatment effect is adjusted by the propensity score.

```
prop.model.adj <- glm(wt82_71 ~ qsmk + p.qsmk.obs, data = nhefshwdat)
summary(prop.model.adj)$coef
```

```
             Estimate Std. Error   t value     Pr(>|t|)
(Intercept)  5.560244  0.5090376 10.923052 8.104078e-27
qsmk         3.397278  0.4559641  7.450757 1.528381e-13
p.qsmk.obs -14.751531  1.8846521 -7.827190 9.128614e-15
```

```
confint(prop.model.adj)
```

```
                2.5 %     97.5 %
(Intercept)  4.562548   6.557939
qsmk         2.503604   4.290951
p.qsmk.obs -18.445381 -11.057680
```

The treatment effect is similar to the stratification method.

Comparing the three methods

The three propensity score methods yield similar results for the treatment effect.

Method	Average Treatment Effect	95% Confidence Interval
Matched	2.93	1.8 - 4.0
Stratified	3.26	1.7 - 3.4
Regression	3.40	2.5 - 4.3
Unadjusted	2.54	1.7 - 3.4

The unadjusted analysis (two-sample t-test) underestimates the treatment effect by approximately 1kg.

Summary

- We use the propensity score in three different ways to calculate the treatment effect in observational studies.
- The three methods were:

1. Matching
2. Stratification and
3. Regression adjustment

- Check that covariates are actually balanced using propensity score methods.
- If covariates are not balanced, then treatment difference might be biased.

Class Outline

- Analysis of Variance (ANOVA) for One-way Classification
  - Blood Coagulation Study Example
  - ANOVA Decomposition
    - ANOVA table
    - ANOVA identity
    - Degrees of freedom and ANOVA table
    - Geometry of ANOVA
    - Two estimates of the population variance
    - Mean Square
    - F Statistic

Comparing more than two treatments

Aim: Design an experiment to compare **more than two** treatments

Previous designs:

Previous designs will not work.

Examples of experiments with more than 2 treatments:

- A clinical trial comparing three drugs A, B, C to reduce duration of intubation for patients on mechanical ventilation.
- Coagulation time of blood samples for animals receiving four different diets A, B, C, D.

What are the null and alternative hypotheses in these two scenarios?

Blood Coagulation Study

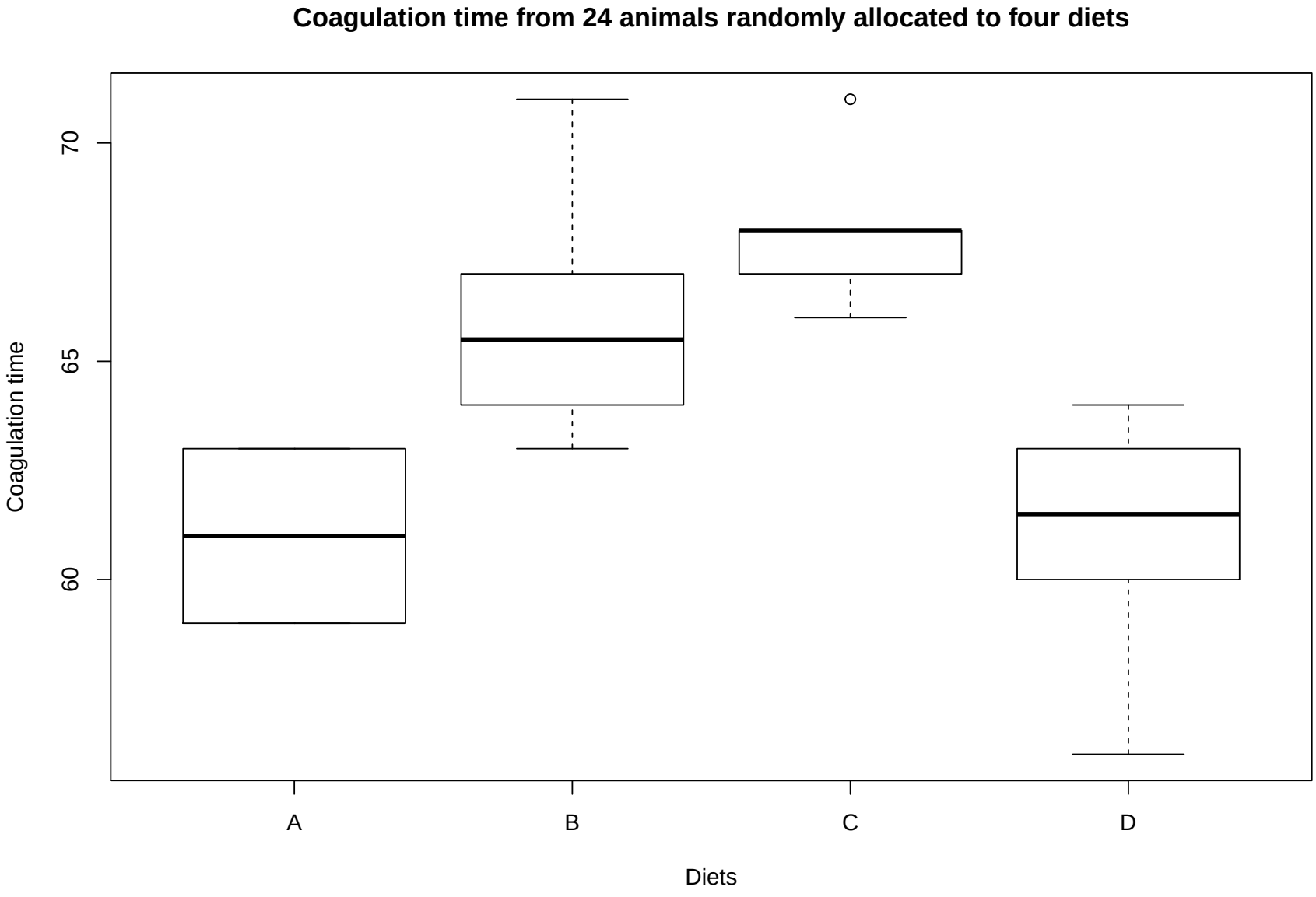
- 24 animals were randomized to four treatments with 6 animals in each group.
- **How many possible treatment assignments?**

Blood Coagulation Study

- The data for coagulation times for blood samples drawn from 24 animals receiving four different diets A, B, C, and D are shown below.

	A	B	C	D	
	60	65	71	62	
	63	66	66	60	
	59	67	68	61	
	63	63	68	64	
	62	64	67	63	
	59	71	68	56	
Treatment Average		61	66	68	61
Grand Average		64	64	64	64
Difference		-3	2	4	-3

Blood Coagulation Study



Do the boxplots show evidence of a difference between diets?

Analysis of Variance (ANOVA)

- An idea due to Fisher is to compare the variation in mean coagulation times *between* the diets to the variation of coagulation times *within* a diet.
- These two measures of variation are often summarized in an analysis of variance (ANOVA) table.
- Fisher introduced the method in his 1925 book "Statistical Methods for Research Workers".
- The statistical procedure enables experimenters to answer several questions at once.
- The prevailing method at the time was to test one factor at a time in an experiment.

Analysis of Variance (ANOVA) table

- The between treatments variation and within treatment variation are two components of the total variation in the response.
- In the coagulation study data we can break up each observation's deviation from the grand mean into two components: treatment deviations; and residuals within treatment deviations.
- Let y_{ij} be the jth $(j = 1, ..., 6)$ observation taken under treatment $i = 1, 2, 3, 4$.

$$y_{ij} - \bar{y}_{\cdot\cdot} = \underbrace{(\bar{y}_{i\cdot} - \bar{y}_{\cdot\cdot})}_{\text{treatment deviation}} + \underbrace{(y_{ij} - \bar{y}_{i\cdot})}_{\text{residual deviation}}$$

$$y_{i\cdot} = \sum_{j=1}^{n} y_{ij}, \qquad \bar{y}_{i\cdot} = y_{i\cdot}/n,$$

$$y_{\cdot\cdot} = \sum_{i=1}^{a}\sum_{j=1}^{n} y_{ij}, \qquad \bar{y}_{\cdot\cdot} = y_{\cdot\cdot}/N,$$

Analysis of Variance (ANOVA) model

- Let y_{ij} be the *jth* observation taken under treatment $i = 1, ..., a$.

$$E(y_{ij}) = \mu_i = \mu + \tau_i,$$

  and $Var(y_{ij}) = \sigma^2$ and the observations are mutually independent.
- The parameter τ_i is the *ith* treatment effect.
- The parameter μ is the overall mean.

Analysis of Variance (ANOVA) model

We are interested in testing if the a treatment means are equal.

$$H_0 : \mu_1 = \cdots = \mu_a \qquad \text{vs.} \qquad H_1 : \mu_i \neq \mu_j,\ i \neq j.$$

There will be n observations under the ith treatment.

$$y_{i\cdot} = \sum_{j=1}^{n} y_{ij}, \qquad \bar{y}_{i\cdot} = y_{i\cdot}/n,$$

$$y_{\cdot\cdot} = \sum_{i=1}^{a}\sum_{j=1}^{n} y_{ij}, \qquad \bar{y}_{\cdot\cdot} = y_{\cdot\cdot}/N,$$

where $N = an$ is the total number of observations. The "dot" subscript notation means sum over the subscript that it replaces.

The ANOVA identity

The total sum of squares $SS_T = \sum_{i=1}^{a} \sum_{j=1}^{n} (y_{ij} - \bar{y}_{..})^2$ can be written as

$$\sum_{i=1}^{a} \sum_{j=1}^{n} [(\bar{y}_{i.} - \bar{y}_{..}) + (y_{ij} - \bar{y}_{i.})]^2$$

by adding and subtracting $\bar{y}_{i.}$ to SS_T.

The ANOVA identity

It can be shown that

$$SS_T = \sum_{i=1}^{a}\sum_{j=1}^{n}(y_{ij} - \bar{y}_{..})^2 = \underbrace{n\sum_{i=1}^{a}(y_{i.} - \bar{y}_{..})^2}_{\text{Sum of Squares Due to Treatment}} + \underbrace{\sum_{i=1}^{a}\sum_{j=1}^{n}(y_{ij} - \bar{y}_{i.})^2}_{\text{Sum of Squares Due to Error}}$$

$$= SS_{Treat} + SS_E.$$

- sometimes called the **analysis of variance identity**
- The total sum of squares can be split into two sum of squares:
  1. due to differences **between** treatments and
  2. due to differences **within** treatments.

The ANOVA identity

	A	B	C	D
	60	65	71	62
	63	66	66	60
	59	67	68	61
	63	63	68	64
	62	64	67	63
	59	71	68	56
Treatment Average	61	66	68	61
Grand Average	64	64	64	64
Difference	-3	2	4	-3

- The decomposition of the first observation $y_{11} = 60$ in diet A is

$$y_{11} - \bar{y}_{\cdot\cdot} = (y_{1\cdot} - \bar{y}_{\cdot\cdot}) + (y_{11} - \bar{y}_{1\cdot})$$
$$60 - 64 = (61 - 64) + (60 - 61)$$
$$-4 = -3 + -1$$

- If each observation is decomposed in this manner then there will be 3 tables of residuals: 1. total residuals, 2. between treatment residuals and 3. within treatment residuals.

Example - Blood coagulation study (SS_T)

The deviations from the grand average ($y_{ij} - \bar{y}_{..}$) are in the table below:

A	B	C	D
-4	1	7	-2
-1	2	2	-4
-5	3	4	-3
-1	-1	4	0
-2	0	3	-1
-5	7	4	-8

The **total sum of squares** is obtained by squaring all the entries in this table and summing: $SS_T = (-4)^2 + (-1)^2 + \cdots + (-8)^2 = 340$.

Example - Blood coagulation study (SS_{Treat})

The **between** treatment deviations ($y_{i\cdot} - \bar{y}_{\cdot\cdot}$) are in the table below:

A	B	C	D
-3	2	4	-3
-3	2	4	-3
-3	2	4	-3
-3	2	4	-3
-3	2	4	-3
-3	2	4	-3

The sum of squares due to treatment is obtained by squaring all the entries in this table and summing: $SS_{Treat} = (-3)^2 + (2)^2 + \cdots + (-3)^2 = 228$.

Example - Blood coagulation study (SS_E)

The **within** treatment deviations $(y_{ij} - \bar{y}_{i\cdot})$ are in the table below:

A	B	C	D
-1	-1	3	1
2	0	-2	-1
-2	1	0	0
2	-3	0	3
1	-2	-1	2
-2	5	0	-5

The sum of squares due to error $(y_{ij} - \bar{y}_{i\cdot})$ is obtained by squaring the entries in this table and summing: $SS_E = (-1)^2 + (2)^2 + \cdots + (-5)^2 = 112$.

$$\underbrace{340}_{SS_T} = \underbrace{228}_{SS_{Treat}} + \underbrace{112}_{SS_E}.$$

-which illustrates the ANOVA identity for the blood coagulation study.

ANOVA - degrees of freedom

- SS_{Treat} is called the sum of squares due to treatments (i.e., between treatments).
- SS_E is called the sum of squares due to error (i.e., within treatments).
- There are $an = N$ total observations. So SS_T has $N - 1$ degrees of freedom.
- There are a treatment levels so SS_{Treat} has $a - 1$ degrees of freedom.
- Within each treatment there are n replicates with $n - 1$ degrees of freedom. There are a treatments. So, there are $a(n - 1) = an - a = N - a$ degrees of freedom for error.

Geometry and the ANOVA Table

- Let a be the vector of deviations from the grand mean,
- Let b be the vector of deviations of treatment deviations
- Let c be the vector of within-treatment deviations.

$a =$(-4, -1, -5, -1, -2, -5, 1, 2, 3, -1, 0, 7, 7, 2, 4, 4, 3, 4, -2, -4, -3, 0, -1, -8),
$b =$(-3, -3, -3, -3, -3, -3, 2, 2, 2, 2, 2, 2, 4, 4, 4, 4, 4, 4, -3, -3, -3, -3, -3, -3),
$c =$(-1, 2, -2, 2, 1, -2, -1, 0, 1, -3, -2, 5, 3, -2, 0, 0, -1, 0, 1, -1, 0, 3, 2, -5).

Geometry and the ANOVA Table

- The dot product of b and c, $b \cdot c$, is

```
b*c
```

```
   A   B   C   D
   3  -2  12  -3
  -6   0  -8   3
   6   2   0   0
  -6  -6   0  -9
  -3  -4  -4  -6
   6  10   0  15
```

```
sum(b*c)
```

```
[1] 0
```

- Therefore, the vectors b and c are orthogonal.
- Thus, the vector a is the hypotenuse of a right triangle with sides b and c.

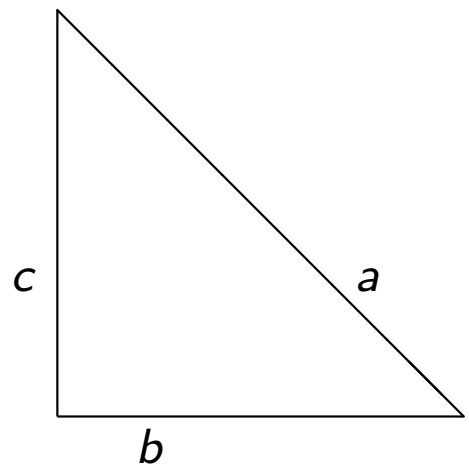
Geometry and the ANOVA Table

Pythagoras' theorem in n dimensions is $|a|^2 = |b|^2 + |c|^2$, where $|a| = \sqrt{a_1^2 + \cdots + a_n^2}$.

The ANOVA identity can be seen using Pythagoras' theorem since

$$|a|^2 = SS_T, |b|^2 = SS_{Treat}, |c|^2 = SS_E.$$

If there were only three observations then the vectors would be as shown below.



The degrees of freedom are the dimensions in which the vectors are free to move given the constraints.

Geometry and the ANOVA Table

Which is/are TRUE?

1. The ANOVA identity SST=SSTreat +SSE assumes that the data follow a normal distribuion.
2. ANOVA is used to compare 2 or more variances.
3. ANOVA is used to compare 2 or more treatment means.
4. The ANOVA identity implies that for each observation, the total residual can be decomposed onto 2 parts: 1. between treatment residual and 2. within treatment residual

ANOVAs Two Estimates of the Population Variance (σ^2)

$$SS_E = \sum_{i=1}^{a} \left[\sum_{j=1}^{n} (y_{ij} - \bar{y}_{i\cdot})^2 \right]$$

If the term inside the brackets is divided by $n-1$ then it is the sample variance for the *ith* treatment

$$S_i^2 = \frac{\sum_{j=1}^{n} (y_{ij} - \bar{y}_{i\cdot})^2}{n-1}, \qquad 1 = 1, ..., a.$$

Combining these a variances to give a single estimate of the common population variance

$$\frac{(n-1)S_1^2 + \cdots + (n-1)S_a^2}{(n-1) + \cdots + (n-1)} = \frac{SS_E}{N-a}.$$

Thus, SS_E is a pooled estimate of the common variance σ^2 within each of the a treatments.

ANOVAs Two Estimates of the Population Variance (σ^2)

If there were no differences between the a treatment means $\bar{y}_{i\cdot}$ we could use the variation of the treatment averages from the grand average to estimate σ^2.

$$\frac{n\sum_{i=1}^{a}(y_{i\cdot}-\bar{y}_{\cdot\cdot})^2}{a-1}=\frac{SS_{Treat}}{a-1}$$

is an estimate of σ^2 when the treatment means are all equal.

ANOVAs Two Estimates of the Population Variance (σ^2)

- The analysis of variance identity gives two estimates of σ^2.
- One is based on the variability **within** treatments and one based on the variability **between** treatments.
- **If there are no differences in the treatment means then these two estimates should be similar.**
- **If these estimates are different then this could be evidence that the difference is due to differences in the treatment means.**

For each plot, which is likely bigger- SSTreat or SSE?

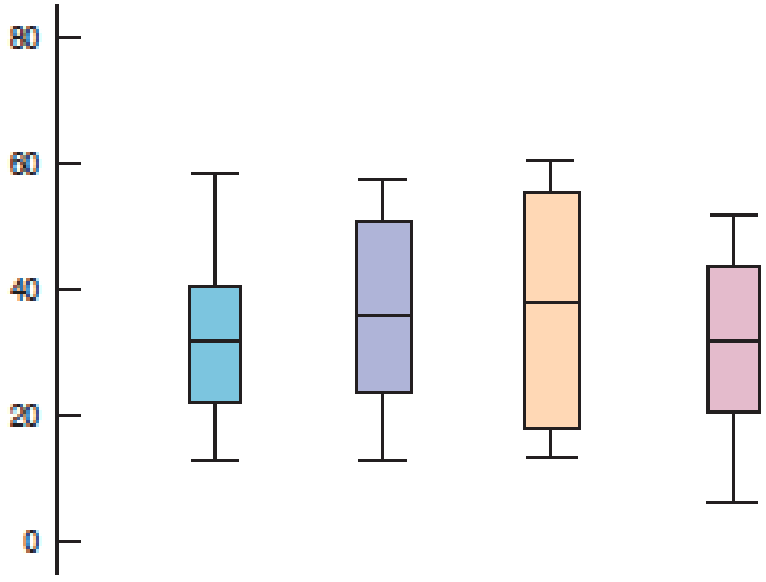


Figure 25.2
It's hard to see the difference in the means in these boxplots because the spreads are large relative to the differences in the means.

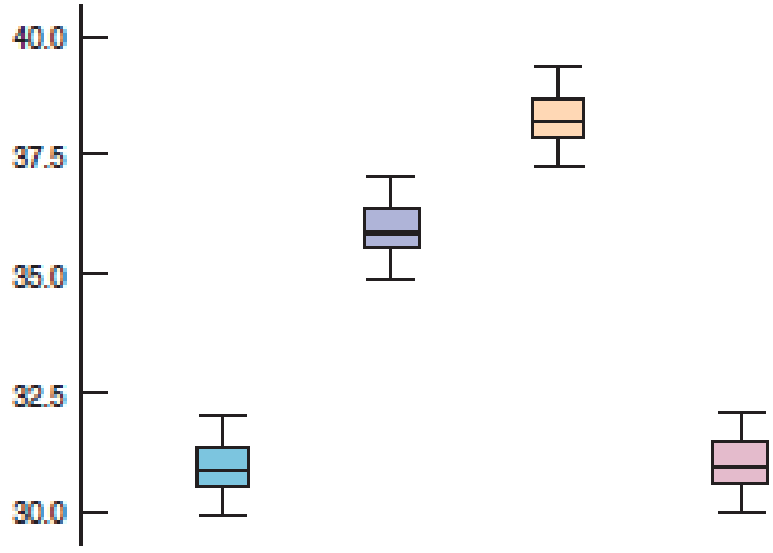


Figure 25.3
In contrast with Figure 25.2, the smaller variation makes it much easier to see the differences among the group means.

Figure: SDM, 2nd Canadian ed. by De Veaux et. al.

ANOVA - Mean square error

The mean square for treatment is defined as

$$MS_{Treat} = \frac{SS_{Treat}}{a-1}$$

and the mean square for error is defined as

$$MS_E = \frac{SS_E}{N-a}.$$

ANOVA - F statistic

- SS_{Treat} and SS_E are independent.
- It can be shown that $SS_{Treat}/\sigma^2 \sim \chi^2_{a-1}$ and $SS_E/\sigma^2 \sim \chi^2_{N-a}$.
- Thus, if $H_0 : \mu_1 = \cdots = \mu_a$ is true then the ratio

$$F = \frac{MS_{Treat}}{MS_E} \sim F_{a-1,N-a}.$$