



# ADVANCED PHARMACEUTICAL BIOSTATISTICS

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Lect 3



Practice: Unpaired T test

Subject #	Female Heights (cm)	Male Height s (cm)	D= Difference
1	171.1	180.4	-15
2	161.0	168.4	-7
3	155.3	170.9	-11
4	167.9	174.1	-13
5	163.8	170.4	-15
MEAN	163.82	172.84	-9.02
SD	6.128	4.695	3.867

$$t = \frac{|\bar{x_1} - \bar{x}|}{\sqrt{\frac{S_1^2}{n_1} + \frac{S_2^2}{n_2}}}$$

$$= \frac{-9.02}{\sqrt{(6.13^{2}/5)+(4.69^{2}/5)}}$$

1

t crit =2.306 (Df=8)





#### t Table

cum. prob one-tail		t.75 0.25	τ <sub>.80</sub> 0.20	t.ss 0.15	t <sub>.90</sub> 0.10	t <sub>.95</sub> 0.05	t <sub>.975</sub> 0.025	t <sub>.99</sub> 0.01	t.995 0.005	<sub>1.999</sub> 0.001	t <sub>.9995</sub>
two-tails	1.00	0.50	0.40	0.30	0.20	0.10	0.05	0.02	0.01	0.002	0.001
df											
1	0.000	1.000	1.376	1.963	3.078	6.314	12.71	31.82	63.66	318.31	636.62
2		0.816	1.061	1.386	1.886	2.920	4.303	6.965	9.925	22.327	31.599
3		0.765	0.978	1.250	1.638	2.353	3.182	4.541	5.841	10.215	12.924
4	1	0.741	0.941	1.190	1.533	2.132	2.776	3.747	4.604	7.173	8.610
5		0.727	0.920	1.156	1.476	2.015	2.571	3.365	4.032	5.893	6.869
6		0.718	0.906	1.134	1.440	1.943	2.447	3.143	3.707	5.208	5.959
7		0.711	0.896	1.119	1.415	1.895	2.365	2.998	3.499	4.785	5.408
8		0.706	0.889	1.108	1.397	1.860	2.306	2.896	3.355	4.501	5.041
9		0.703	0.883	1.100	1.383	1.833	2.262	2.821	3.250	4.297	4.781
10		0.700	0.879	1.093	1.372	1.812	2.228	2.764	3.169	4.144	4.587
11	1	0.697	0.876	1.088	1.363	1.796	2.201	2.718	3.106	4.025	4.437
12		0.695	0.873	1.083	1.356	1.782	2.179	2.681	3.055	3.930	4.318
13	1	0.694	0.870	1.079	1.350	1.771	2.160	2.650	3.012	3.852	4.221
14 15		0.692	0.868	1.076	1.345	1.761	2.145	2.624	2.977	3.787	4.140
15		0.691 0.690	0.866 0.865	1.074 1.071	1.341 1.337	1.753 1.746	2.131 2.120	2.602 2.583	2.947 2.921	3.733 3.686	4.073 4.015
10		0.689	0.863	1.069	1.337	1.740	2.120	2.563	2.898	3.646	3.965
17		0.688	0.862	1.069	1.333	1.740	2.10	2.557	2.878	3.640	3.905
19		0.688	0.861	1.066	1.328	1.729	2.093	2.532	2.861	3.579	3.883
20		0.687	0.860	1.064	1.325	1.725	2.095	2.539	2.845	3.552	3.850
21		0.686	0.859	1.063	1.323	1.721	2.080	2.518	2.831	3.527	3.819
22		0.686	0.858	1.061	1.321	1.717	2.074	2.508	2.819	3.505	3.792
23		0.685	0.858	1.060	1.319	1.714	2.069	2.500	2.807	3.485	3.768
24		0.685	0.857	1.059	1.318	1.711	2.064	2.492	2.797	3.467	3.745
25		0.684	0.856	1.058	1.316	1.708	2.060	2.485	2.787	3.450	3.725
26		0.684	0.856	1.058	1.315	1.706	2.056	2.479	2.779	3.435	3.707
27		0.684	0.855	1.057	1.314	1.703	2.052	2.473	2.771	3.421	3.690
28	0.000	0.683	0.855	1.056	1.313	1.701	2.048	2.467	2.763	3.408	3.674
29	0.000	0.683	0.854	1.055	1.311	1.699	2.045	2.462	2.756	3.396	3.659
30	0.000	0.683	0.854	1.055	1.310	1.697	2.042	2.457	2.750	3.385	3.646
40		0.681	0.851	1.050	1.303	1.684	2.021	2.423	2.704	3.307	3.551
60	1	0.679	0.848	1.045	1.296	1.671	2.000	2.390	2.660	3.232	3.460
80		0.678	0.846	1.043	1.292	1.664	1.990	2.374	2.639	3.195	3.416
100		0.677	0.845	1.042	1.290	1.660	1.984	2.364	2.626	3.174	3.390
1000	0.000	0.675	0.842	1.037	1.282	1.646	1.962	2.330	2.581	3.098	3.300
z	0.000	0.674	0.842	1.036	1.282	1.645	1.960	2.326	2.576	3.090	3.291
	0%	50%	60%	70%	80%	90%	95%	98%	99%	99.8%	99.9%

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• Practice: paired T test

Subject #	Heart Rate (Resting) Beats/min	Heart Rate (After Exercise) Beats/min	D= Difference
1	70	85	-15.0
2	74	81	-7.0
3	68	79	-11.0
4	55	68	-13.0
5	80	95	-15.0
MEAN	69.4	81.6	-12.2
SE	4.14	4.38	1.50

$$t = \frac{\overline{D}}{SE_D}$$

$$t = \frac{-12.2}{1.5}$$

t crit =2.776 (Df=4)



**Example: Effect of exercise on heart rate?** 

• Practice: one sample T test

Subject #	Human IQ	Averag e normal	D= Difference	$t = \frac{X - M}{SE_1}$
1	85			$t = \frac{35.7}{1}$
2	120			6.37
3	90			<i>t</i> = 5.61
4	105	100		t crit =1.833 (Df=9)
5	110			
MEAN	135		35.7	
SE	6.37			







# **Analysis of Variance**

Family of hypothesis tests for comparing multiple (3+) sample groups.

ANOVA tests compare the means of one or more **dependent** variables, measured from groups of subjects categorised according to one or more **independent variables (factors)**, representing different treatments or properties of the within each group.



### Dependent Variable (or response)

The measured experimental variable of interest which are affected by the factors.

e.g. weight, blood pressure, heart rate.

### Factor (or independent variable)

Variable (usually nominal) representing the factors that affect the dependent variable

e.g. gender, treatment

### Levels (of the factor)

Individual values of the factor variable representing the treatment or property used to categorise the subjects into groups. e.g. The gender factor would have 2 levels: Male & Female.





# Common Types of Analysis of Variance One way ANOVA

#### Single factor, multiple levels.

Compares differences between means of 3 or more <u>independent</u> groups of subjects

### One way (repeated measures) ANOVA

Single factor, multiple levels

Compares differences between means of 3 or more groups of measurements repeatedly made on the <u>same</u> subjects

### Two way ANOVA

Two factors, multiple levels.

Determines whether each of the two factors have an effect on the dependent variable and whether there is interaction between the factors. May be independent subjects, repeated measures or mixed.

# **One way ANOVA**

Four gps of patients were subjected to 4 different physical treatments therapy abd at end the following scores were obtained . Analysis the treatment effectiveness

	TR A	TR B	TR C	TR D	
	64	76	58	95	
	88	70	74	90	
	72	90	66	80	
	80	80	60	87	
	79	75	82	88	
	71	82	75	85	
Sum	454	473	415	525	1867
Mean	75.7	78.8	69.2	87.5	

1- Ground total =1867  
2- Mean of All 
$$\overline{\mathbf{x}}$$
 = 1867/24= 77.9  
3- Corr. Factor = $\frac{(\Sigma(\Sigma x))^2}{24}$ = 145237.04  
4-Total SS = $(\Sigma(X^2))$ - CF =2201.96  
5-between Tr ss= $\frac{\Sigma((\Sigma X)^2)}{6}$  - CF= $\frac{254^2+254^2+254^2+254^2}{6}$  - CF  
= 1045.46  
6- within tr ss= total ss - bet Tr ss=2201.96-1045.46  
= 1156.5

SOURCE OF VARIANCE	D.F	SS	Ms (Mean Squre) =ss/D.F	F =ms/ms	Table 0.05	Table 0.01
Bet gps	3	1045.46	348.5	6.03	3.1	4.94
Withn gps	20	1156.5	57.83			
total	23					







	DF1	α = 0.05																	
DF2	1	2	3	4	5	6	7	8	9	10	12	15	20	24	30	40	60	120	Inf
1	161.45	199.5	215.71	224.58	230.16	233.99	236.77	238.88	240.54	241.88	243.91	245.95	248.01	249.05	250.1	251.14	252.2	253.25	254.31
2	18.513	19	19.164	19.247	19.296	19.33	19.353	19.371	19.385	19.396	19.413	19.429	19.446	19.454	19.462	19.471	19.479	19.487	19.496
3	10.128	9.5521	9.2766	9.1172	9.0135	8.9406	8.8867	8.8452	8.8123	8.7855	8.7446	8.7029	8.6602	8.6385	8.6166	8.5944	8.572	8.5494	8.5264
4	7.7086	6.9443	6.5914	6.3882	6.2561	6.1631	6.0942	6.041	5.9988	5.9644	5.9117	5.8578	5.8025	5.7744	5.7459	5.717	5.6877	5.6581	5.6281
5	6.6079	5.7861	5.4095	5.1922	5.0503	4.9503	4.8759	4.8183	4.7725	4.7351	4.6777	4.6188	4.5581	4.5272	4.4957	4.4638	4.4314	4.3985	4.365
6	5.9874	5.1433	4.7571	4.5337	4.3874	4.2839	4.2067	4.1468	4.099	4.06	3.9999	3.9381	3.8742	3.8415	3.8082	3.7743	3.7398	3.7047	3.6689
7	5.5914	4.7374	4.3468	4.1203	3.9715	3.866	3.787	3.7257	3.6767	3.6365	3.5747	3.5107	3.4445	3.4105	3.3758	3.3404	3.3043	3.2674	3.2298
8	5.3177	4.459	4.0662	3.8379	3.6875	3.5806	3.5005	3.4381	3.3881	3.3472	3.2839	3.2184	3.1503	3.1152	3.0794	3.0428	3.0053	2.9669	2.9276
9	5.1174	4.2565	3.8625	3.6331	3.4817	3.3738	3.2927	3.2296	3.1 <b>78</b> 9	3.1373	3.0729	3.0061	2.9365	2.9005	2.8637	2.8259	2.7872	2.7475	2.7067
10	4.9646	4.1028	3.7083	3.478	3.3258	3.2172	3.1355	3.0717	3.0204	2.9782	2.913	2.845	2.774	2.7372	2.6996	2.6609	2.6211	2.5801	2.5379
11	4.8443	3. <b>9</b> 823	3.5874	3.3567	3.2039	3 <b>.094</b> 6	3.0123	2.948	2.8962	2.8536	2.7876	2.7186	2.6464	2.609	2.5705	2.5309	2.4901	2.448	2.4045
12	4.7472	3. <b>8</b> 853	3.4903	3.2592	3.1059	2.9961	2.9134	2.8486	2.7964	2.7534	2.6866	2.6169	2.5436	2.5055	2.4663	2.4259	2.3842	2.341	2.2962
13	4.6672	3.8056	3.4105	3.1791	3.0254	2.9153	2.8321	2.7669	2.7144	2.671	2.6037	2.5331	2.4589	2.4202	2.3803	2.3392	2.2966	2.2524	2.2064
14	4.6001	3.7389	3.3439	3.1122	2.9582	2.8477	2.7642	2.6987	2.6458	2.6022	2.5342	2.463	2.3879	2.3487	2.3082	2.2664	2.2229	2.1778	2.1307
15	4.5431	3.6823	3.2874	3.0556	2.9013	2.7905	2.7066	2.6408	2.5876	2.5437	2.4753	2.4034	2.3275	2.2878	2.2468	2.2043	2.1601	2.1141	2.0658
16	4.494	3. <b>6</b> 337	3.2389	3.0069	2.8524	2.7413	2.6572	2.5911	2.5377	2.4935	2.4247	2.3522	2.2756	2.2354	2.1938	2.1507	2.1058	2.0589	2.0096
17	4.4513	3.5915	3.1968	2.9647	2.81	2.6987	2.6143	2.548	2.4943	2.4499	2.3807	2.3077	2.2304	2.1898	2.1477	2.104	2.0584	2.0107	1.9604
18	4.4139	3.5546	3.1599	2.9277	2.7729	2.6613	2.5767	2.5102	2.4563	2.4117	2.3421	2.2686	2.1906	2.1497	2.1071	2.0629	2.0166	1.9681	1.9168
19	4.3807	3.5219	3.1274	2,8951	2.7401	2.6283	2.5435	2.4768	2.4227	2.3779	2.308	2.2341	2.1555	2.1141	2.0712	2.0264	1.9795	1.9302	1.878
20	4.3512	3.4928	3.0984	2.8661	2.7109	2.599	2.514	2.4471	2.3928	2.3479	2.2776	2.2033	2.1242	2.0825	2.0391	1.9938	1.9464	1.8963	1.8432
21	4.3248	3.4668	3.0725	28401	2.6848	2.5727	2.4876	2.4205	2.366	2.321	2.2504	2.1757	2.096	2.054	2.0102	1.9645	1.9165	1.8657	1.8117
22	4.3009	3.4434	3.0491	2.8167	2.6613	2.5491	2.4638	2.3965	2.3419	2.2967	2.2258	2.15 <b>0</b> 8	2.0707	2.0283	1.9842	1.938	1.8894	1.838	1.7831
23	4.2793	3.4221	3.028	2.7955	2.64	2.5277	2.4422	2.3748	2.3201	2.2747	2.2036	2.1282	2.0476	2.005	1.9605	1.9139	1.8648	1.8128	1.757
24	4.2597	3.4028	3.0088	2.7763	2.6207	2.5082	2.4226	2.3551	2.3002	2.2547	2.1834	2.1077	2.0267	1.9838	1.939	1.892	1.8424	1.7896	1.733
25	4.2417	3.3852	2.9912	2.7587	2.603	2.4904	2.4047	2.3371	2.2821	2.2365	2.1649	2.0889	2.0075	1.9643	1.9192	1.8718	1.8217	1.7684	1.711
26	4.2252	3.369	2.9752	2.7426	2.5868	2.4741	2.3883	2.3205	2.2655	2.2197	2.1479	2.0716	1.9898	1.9464	1.901	1.8533	1.8027	1.7488	1.6906
27	4.21	3.3541	2.9604	2.7278	2.5719	2.4591	2.3732	2.3053	2.2501	2.2043	2.1323	2.0558	1.9736	1.9299	1.8842	1.8361	1.7851	1.7306	1.6717
28	4.196	3.3404	2.9467	2.7141	2.5581	2.4453	2.3593	2.2913	2.236	2.19	2.1179	2.0411	1.9586	1.9147	1.8687	1.8203	1.7689	1.7138	1.6541
29	4.183	3.3277	2.934	2.7014	2.5454	2.4324	2.3463	2.2783	2.2229	2.1768	2.1045	2.0275	1.9446	1.9005	1.8543	1.8055	1.7537	1.6981	1.6376
30	4.1709	3.3158	2.9223	2.6896	2.5336	2.4205	2.3343	2.2662	2.2107	2.1646	2.0921	2.0148	1.9317	1.8874	1.8409	1.7918	1.7396	1.6835	1.6223
40	4.0847	3.2317	2.8387	2.606	2.4495	2.3359	2.249	2.1802	2.124	2.0772	2.0035	1.9245	1.8389	1.7929	1.7444	1.6928	1.6373	1.5766	1.5089
60	4.0012	3.1504	2.7581	2.5252	2.3683	2.2541	2.1665	2.097	2.0401	1.9926	1.9174	1.8364	1.748	1.7001	1.6491	1.5943	1.5343	1.4673	1.3893
120	3.9201	3.0718	2.6802	2.4472	2.2899	2.175	2.0868	2.0164	1.9588	1.9105	1.8337	1.7505	1.6587	1.6084	1.5543	1.4952	1.429	1.3519	1.2539
Inf	3.8415	2.9957	2.6049	2.3719	2.2141	2.0986	2.0096	1.9384	1.8799	1.8307	1.7522	1.6664	1.5705	1.5173	1.4591	1.394	1.318	1.2214	1





Excell

ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	1045.46	3	348. 5	6.03	0.004	3.098
Within Groups	1156.5	20	57.825			
Total	2201.958	23				

#### Minitab

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Factor	3	1045	348.49	6.03	0.004
Error	20	1157	57.83		
Total	23	2202			



## Least significant difference

$$LSD_{0.05} = \sqrt{\frac{2(MS)}{n}} = \sqrt{\frac{2(57.83)}{6}} = 4.39$$

C.V= 
$$\sqrt{\frac{MS}{X}}$$
. 100%= $\frac{57.83}{77.8}$ . 100% = 9.77%

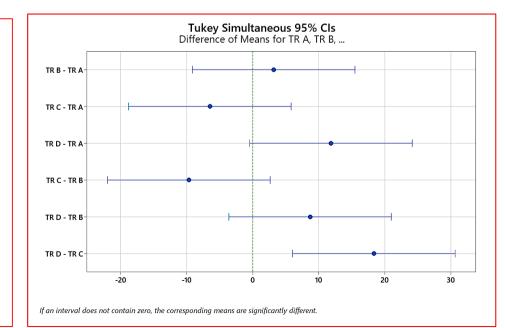
TR	Mean	relation
С	69.2	C-A=6.4, C-B= <mark>9.7</mark> , C-D= <mark>18.3</mark>
А	75.6	A-B =1.2 , A-D= <mark>11.8</mark> , C-A=6.4
В	78.8	B-D=8.7, B-C= <mark>9.7 ,</mark> B-A =1.2
D	87.5	D-C= <mark>18.3,</mark> D-A = <mark>11.8</mark> , B-D=8.7

No. of comp	parisons for give	en group size
$n_{comparisons} = -$	$n_{grps} \times (n_{grps} - 1)$	$6 = \frac{4 \times 3}{2}$
	2	2

#### **Tukey Simultaneous Tests for Differences of Means**

Difference	Difference	SE of			Adjusted
of Levels	of Means	Difference	95% CI	T-Value	P-Value
TR B - TR A	3.17	4.39	(-9.13, 15.46)	0.72	0.887
TR C - TR A	-6.50	4.39	(-18.79, 5.79)	-1.48	0.467
TR D - TR A	11.83	4.39	(-0.46, 24.13)	2.70	0.062
TR C - TR B	-9.67	4.39	(-21.96, 2.63)	-2.20	0.157
TR D - TR B	8.67	4.39	(-3.63, 20.96)	1.97	0.231
TR D - TR C	18.33	4.39	(6.04, 30.63)	4.18	0.002

Individual confidence level = 98.89%





## Least significant difference

$$LSD_{0.05} = \sqrt{\frac{2(MS)}{n}} = \sqrt{\frac{2(57.83)}{6}} = 9.16$$

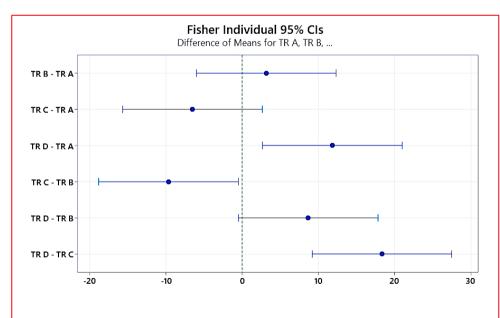
C.V= 
$$\sqrt{\frac{MS}{X}}$$
. 100%= $\frac{57.83}{77.8}$ . 100% = 9.77%

TR	Mean	relation
С	69.2	C-A=6.4, C-B= <mark>9.7</mark> , C-D= <mark>18.3</mark>
А	75.6	A-B =1.2 , A-D= <mark>11.8</mark> , C-A=6.4
В	78.8	B-D=8.7, B-C= <mark>9.7 ,</mark> B-A =1.2
D	87.5	D-C= <mark>18.3,</mark> D-A = <mark>11.8</mark> , B-D=8.7

#### **Fisher Individual Tests for Differences of Means**

Difference Difference		SE of			Adjusted
of Levels	of Means	Difference	95% CI	T-Value	P-Value
TR B - TR A	3.17	4.39	(-5.99, 12.32)	0.72	0.479
TR C - TR A	-6.50	4.39	(-15.66, 2.66)	-1.48	0.154
TR D - TR A	11.83	4.39	(2.68, 20.99)	2.70	0.014
TR C - TR B	-9.67	4.39	(-18.82, -0.51)	-2.20	0.040
TR D - TR B	8.67	4.39	(-0.49, 17.82)	1.97	0.062
TR D - TR C	18.33	4.39	(9.18, 27.49)	4.18	0.000

Simultaneous confidence level = 80.83%



If an interval does not contain zero, the corresponding means are significantly different.





Example: Investigation of the effects of a diet and/or exercise program on body weight. Test subjects split into 4 groups.

Group Code	Treatment	No. Subjects
С	No dieting, no exercise (control group)	5
D	Dieting, no exercise	5
E	Exercise, no dieting	5
DE	Dieting + exercise	5

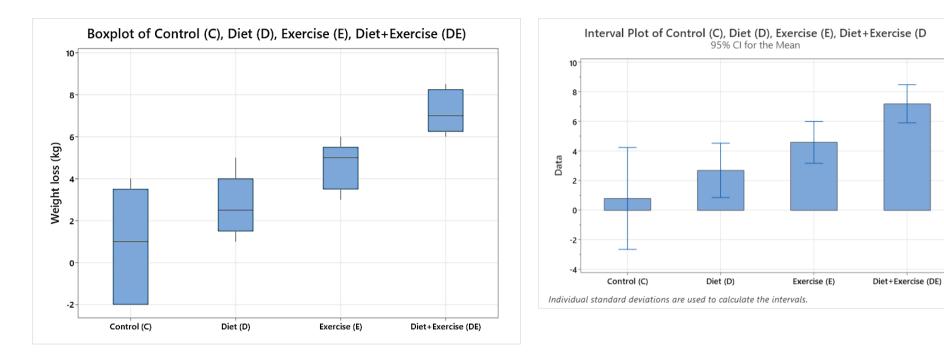




#### Effect of diet/exercise on weight: Results

Group	Weight Loss (kg)						
						Avg.	
Control (C)	3	4	-2	1	-2	0.34	
Diet (D)	5	3	2	1	2.5	2.94	
Exercise (E)	6	4	5	3	5	4.6	
Diet+Exercise (DE)	8	7	6	6.5	8.5	7.2	







#### **Effect of diet/exercise on weight loss?**



### 4 Groups

Control, Diet, Exercise, Diet+Exercise Dependent Variable Weight loss Independent Variable Treatment: Control / Diet / Exercise / Exercise+Diet

# Possible Comparisons (6)

Control vs. Diet Control vs. Exercise Control vs. Diet + Exercise Diet vs. Exercise Diet vs. Diet + Exercise Exercise vs. Diet + Exercise

Do any of the treatments work?

Which is better?

No. of comparisons for given group size  $n_{comparisons} = \frac{n_{grps} \times (n_{grps} - 1)}{2} \qquad 6 = \frac{4 \times 3}{2}$ 



#### **Analysis of Variance**

Source DF Adj SS Adj MS F-Value P-Value

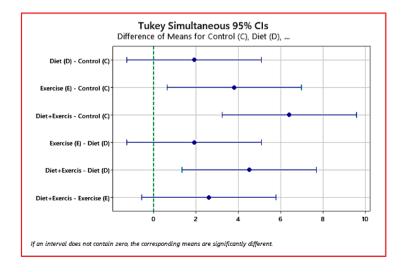


Factor3112.0437.34612.170.000Error1649.103.069Total19161.14

#### **Tukey Simultaneous Tests for Differences of Means**

	Difference	SE of			Adjusted
Difference of Levels	of Means Dif	ference	95% CI	T-Value	P-Value
Diet (D) - Control (C)	1.90	1.11	(-1.27, 5.07)	1.71	0.348
Exercise (E) - Control (C)	3.80	1.11	(0.63, 6.97)	3.43	0.016
Diet+Exercis - Control (C)	6.40	1.11	(3.23, 9.57)	5.78	0.000
Exercise (E) - Diet (D)	1.90	1.11	(-1.27, 5.07)	1.71	0.348
Diet+Exercis - Diet (D)	4.50	1.11	(1.33, 7.67)	4.06	0.005
Diet+Exercis - Exercise (E)	2.60	1.11	(-0.57, 5.77)	2.35	0.129

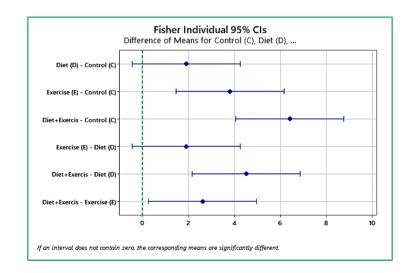
Individual confidence level = 98.87%



#### Fisher Individual Tests for Differences of Means

	Difference	SE of			Adjusted
Difference of Levels	of Means D	oifference	95% CI	T-Value	P-Value
Diet (D) - Control (C)	1.90	1.11	(-0.45, 4.25)	1.71	0.106
Exercise (E) - Control (C)	3.80	1.11	(1.45, 6.15)	3.43	0.003
Diet+Exercis - Control (C)	6.40	1.11	(4.05, 8.75)	5.78	0.000
Exercise (E) - Diet (D)	1.90	1.11	(-0.45, 4.25)	1.71	0.106
Diet+Exercis - Diet (D)	4.50	1.11	(2.15, 6.85)	4.06	0.001
Diet+Exercis - Exercise (E)	2.60	1.11	(0.25, 4.95)	2.35	0.032

Simultaneous confidence level = 81.11%





 $\mathsf{LSD}_{0.05} = \sqrt{\frac{2(MS)}{n}}$ 

Significant differences between groups indicated by asterisks and lines joining bars

\* P < 0.05 \*\* P < 0.01

