

Appendix 3

19:53 Monday, December 11, 2006 1301

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

T0 = Baseline (A Covariate)

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
16	2	80.98119040	429.89241035
17	2	77.44134478	66.37824695
18	2	76.21439444	54.18644007
19	2	73.41194465	22.53141329
20	3	71.12298748	.
21	1	69.74406030	0.00577082
22	1	68.95135126	0.00122298
23	1	68.78931330	0.00014043
24	1	68.77186353	0.00000368
25	1	68.77143827	0.00000000

Convergence criteria met.

Estimated R Matrix  
for Subject 1

Row	Col1	Col2
1	0.002081	0.000415
2	0.000415	0.002081

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
STUDY			0.006106
STUDY*TREAT			0.009140

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## The Mixed Procedure

## Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
Variance	PATIENT(STUDY)	STUDY 2	0.001665
CS	PATIENT(STUDY)	STUDY 2	0.000415
Variance	PATIENT(STUDY)	STUDY 3	0.1241
CS	PATIENT(STUDY)	STUDY 3	-0.00823
Variance	PATIENT(STUDY)	STUDY 4	0.1268
CS	PATIENT(STUDY)	STUDY 4	-0.03031
Variance	PATIENT(STUDY)	STUDY 6	0.1610
CS	PATIENT(STUDY)	STUDY 6	0.04139
Variance	PATIENT(STUDY)	STUDY 7	0.04564
CS	PATIENT(STUDY)	STUDY 7	0.09943

## Fit Statistics

-2 Res Log Likelihood	68.8
AIC (smaller is better)	92.8
AICC (smaller is better)	94.9
BIC (smaller is better)	88.1

## PARMS Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
12	153.36	<.0001

## Meta-Analysis of Phenylephrine vs. Placebo

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## The Mixed Procedure

## Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
TO	1	94.7	6.82	0.0105
TREAT	1	2.57	0.33	0.6129

## Least Squares Means

Effect	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	-0.2754	0.06686	6.94	-4.12	0.0046	0.05	-0.4338	-0.1170
TREAT	Placebo	-0.2298	0.06694	6.94	-3.43	0.0111	0.05	-0.3884	-0.07126

## Differences of Least Squares Means

Effect	TREAT	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	Placebo	-0.04557	0.07954	2.57	-0.57	0.6129	0.05	-0.3243	0.2331

Meta-Analysis of Phenylephrine vs. Placebo

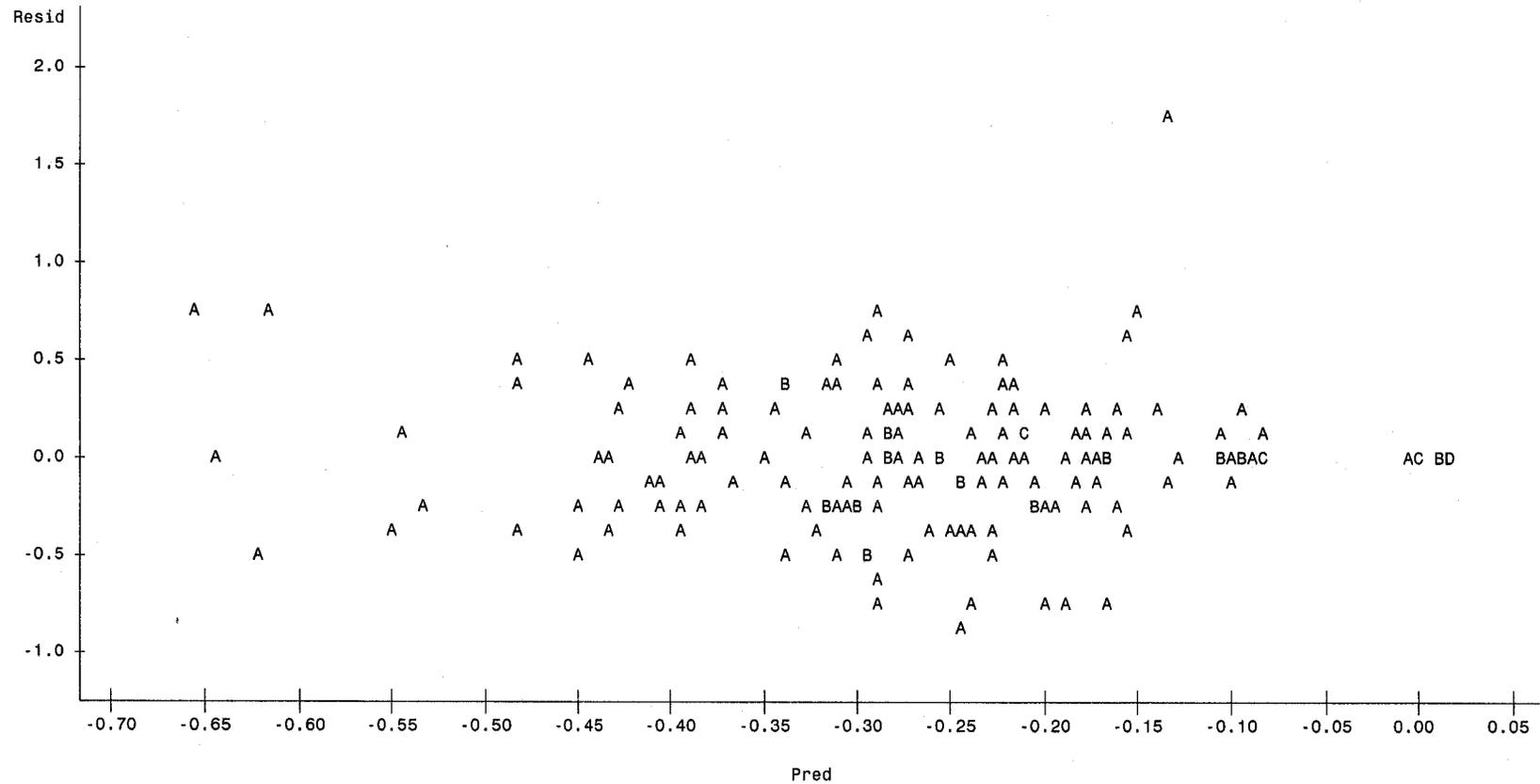
Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

T0 = Baseline (A Covariate)

Plot of Resid\*Pred. Legend: A = 1 obs, B = 2 obs, etc.



Meta-Analysis of Phenylephrine vs. Placebo

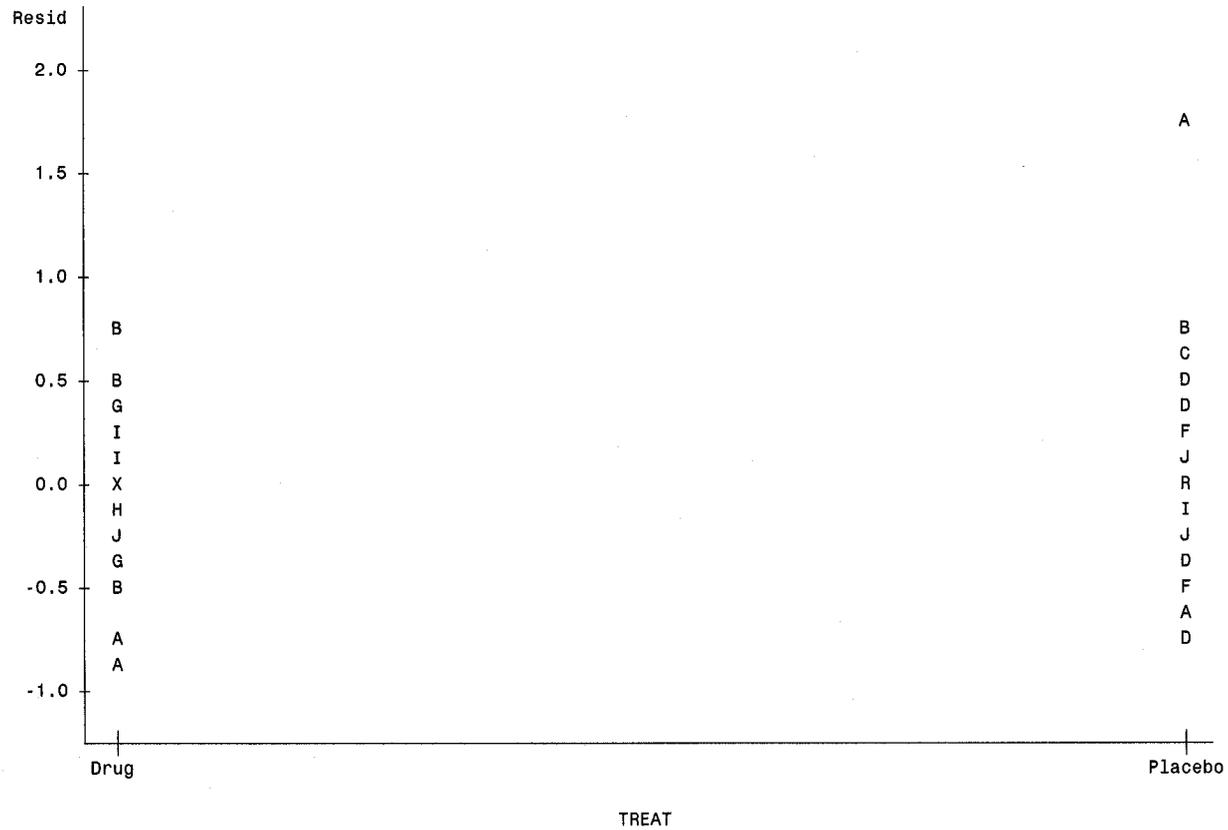
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TO = Baseline (A Covariate)

Plot of Resid\*TREAT. Legend: A = 1 obs, B = 2 obs, etc.



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Drug -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	-0.0032734	Sum Observations	-0.2684148
Std Deviation	0.28738456	Variance	0.08258989
Skewness	-0.0252871	Kurtosis	0.79878991
Uncorrected SS	6.69065942	Corrected SS	6.68978081
Coeff Variation	-8779.5209	Std Error Mean	0.03173632

## Basic Statistical Measures

Location		Variability	
Mean	-0.00327	Std Deviation	0.28738
Median	-0.02379	Variance	0.08259
Mode	.	Range	1.64374
		Interquartile Range	0.37703

## Tests for Location: MU0=0

Test	-Statistic-	-----p Value-----
Student's t	t -0.10314	Pr >  t  0.9181
Sign	M -6	Pr >=  M  0.2242
Signed Rank	S -53.5	Pr >=  S  0.8064

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

## The UNIVARIATE Procedure

Variable: Resid

## Tests for Normality

Test	--Statistic---	-----p Value-----
Shapiro-Wilk	W 0.987567	Pr < W 0.6191
Kolmogorov-Smirnov	D 0.07855	Pr > D >0.1500
Cramer-von Mises	W-Sq 0.074841	Pr > W-Sq 0.2424
Anderson-Darling	A-Sq 0.394257	Pr > A-Sq >0.2500

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	0.8072881
99%	0.8072881
95%	0.4200104
90%	0.3209037
75% Q3	0.1868179
50% Median	-0.0237895
25% Q1	-0.1902116
10%	-0.3502912
5%	-0.4367714
1%	-0.8364516
0% Min	-0.8364516

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.836452	7020	52	0.420010	7002	43
-0.727484	7036	61	0.491429	3023	74
-0.492060	3036	77	0.493342	4017	6
-0.456126	3001	67	0.694196	7042	63
-0.436771	3015	72	0.807288	7018	51

Meta-Analysis of Phenylephrine vs. Placebo

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Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

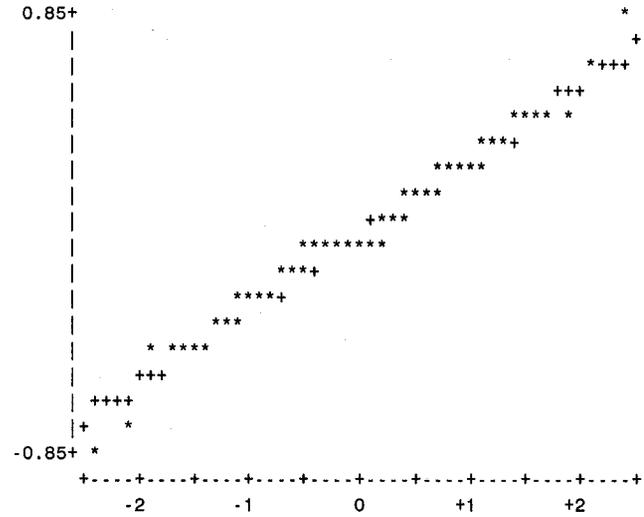
Stem Leaf	#
8 1	1
7	
6 9	1
5	
4 00299	5
3 1226	4
2 122355889	9
1 01255679	8
0 1235668	7
-0 9877655544444333211100	22
-1 97544	5
-2 876653210	9
-3 6522	4
-4 96422	5
-5	
-6	
-7 3	1
-8 4	1

-----+-----+-----+-----+  
 Multiply Stem.Leaf by 10\*\*-.1

Boxplot



Normal Probability Plot



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

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Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	-0.0037079	Sum Observations	-0.3040449
Std Deviation	0.39746523	Variance	0.15797861
Skewness	0.95130781	Kurtosis	3.73302584
Uncorrected SS	12.7973949	Corrected SS	12.7962676
Coeff Variation	-10719.517	Std Error Mean	0.04389269

## Basic Statistical Measures

Location		Variability	
Mean	-0.00371	Std Deviation	0.39747
Median	-0.00812	Variance	0.15798
Mode	-0.01035	Range	2.53518
		Interquartile Range	0.40373

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----	
Student's t	t -0.08448	Pr >  t	0.9329
Sign	M -2	Pr >=  M	0.7407
Signed Rank	S -98.5	Pr >=  S	0.6517

## Meta-Analysis of Phenylephrine vs. Placebo

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T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Tests for Normality

Test		--Statistic--		-----p Value-----
Shapiro-Wilk	W	0.941136	Pr < W	0.0009
Kolmogorov-Smirnov	D	0.094733	Pr > D	0.0692
Cramer-von Mises	W-Sq	0.126992	Pr > W-Sq	0.0480
Anderson-Darling	A-Sq	0.731107	Pr > A-Sq	0.0558

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	1.75590374
99%	1.75590374
95%	0.65134761
90%	0.47652296
75% Q3	0.16509420
50% Median	-0.00811963
25% Q1	-0.23863452
10%	-0.48057555
5%	-0.60543081
1%	-0.77927606
0% Min	-0.77927606

## Meta-Analysis of Phenylephrine vs. Placebo

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T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.779276	7034	60	0.651348	6005	18
-0.776560	3036	77	0.657585	7028	56
-0.743555	6041	28	0.695748	7042	63
-0.707373	6017	22	0.712978	4037	13
-0.605431	7016	49	1.755904	6026	24

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----- TREAT=Placebo -----

The UNIVARIATE Procedure  
Variable: Resid

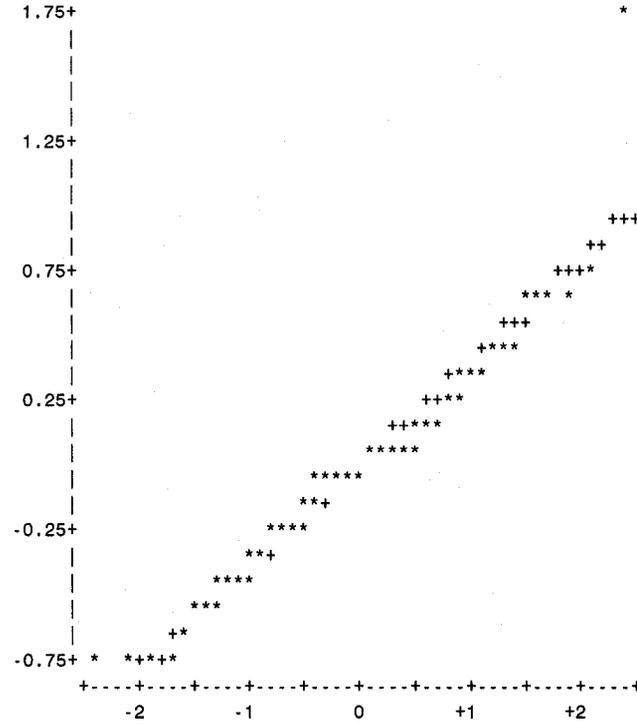
Stem Leaf	#
17 6	1
16	
15	
14	
13	
12	
11	
10	
9	
8	
7 01	2
6 556	3
5 0	1
4 488	3
3 13346	5
2 6789	4
1 4566679	7
0 0012344566779	13
-0 98887642211110	14
-1 8821	4
-2 96443110	8
-3 4200	4
-4 86411	5
-5 653	3
-6 1	1
-7 8841	4
-----+-----+-----+-----+	

Multiply Stem.Leaf by 10\*\*-1

Boxplot



Normal Probability Plot





## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

The Mixed Procedure

## Model Information

Data Set	WORK.TEN_MG
Dependent Variable	LN180CHG
Covariance Structure	Variance Components
Group Effect	STUDY
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Prasad-Rao-Jeske- Kackar-Harville
Degrees of Freedom Method	Kenward-Roger

## Class Level Information

Class	Levels	Values
TREAT	2	Drug Placebo
STUDY	5	2 3 4 6 7

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## The Mixed Procedure

## Class Level Information

Class	Levels	Values
PATIENT	82	2001 2005 2007 2012 2014 2018 2020 2021 2023 2024 3001 3003 3005 3008 3009 3015 3018 3023 3026 3032 3036 3039 3041 3044 3046 3048 4001 4003 4007 4010 4012 4017 4024 4026 4027 4030 4032 4034 4037 4039 4044 6001 6003 6005 6008 6010 6013 6017 6023 6026 6031 6034 6040 6041 6044 6046 6048 7001 7002 7003 7007 7008 7010 7014 7016 7017 7018 7020 7021 7025 7027 7028 7030 7031 7033 7034 7036 7041 7042 7044 7048 7050

## Dimensions

Covariance Parameters	5
Columns in X	101
Columns in Z	0
Subjects	164
Max Obs Per Subject	1
Observations Used	164
Observations Not Used	0
Total Observations	164

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Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

The Mixed Procedure

## Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	103.19985669	
1	2	70.10810466	0.00002666
2	1	70.10716497	0.00000001
3	1	70.10716457	0.00000000

Convergence criteria met.

## Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	STUDY 2	0.001628
Residual	STUDY 3	0.1146
Residual	STUDY 4	0.1337
Residual	STUDY 6	0.1205
Residual	STUDY 7	0.04761

## Fit Statistics

-2 Res Log Likelihood	70.1
AIC (smaller is better)	80.1
AICC (smaller is better)	81.0
BIC (smaller is better)	95.6

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)

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Assuming Within Subject Variance Component Differs Across Studies

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## The Mixed Procedure

## Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
4	33.09	<.0001

## Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
TO	1	67.7	11.64	0.0011
PATIENT(STUDY)	77	25.5	2.28	0.0107
STUDY	4	35	2.93	0.0344
TREAT	1	49.7	0.85	0.3604
TREAT*STUDY	4	30.5	3.08	0.0305

## Least Squares Means

Effect	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
STUDY		2	-0.2529	0.06289	67.3	-4.02	0.0001	0.05	-0.3784	-0.1274
STUDY		3	-0.4261	0.06144	16	-6.94	<.0001	0.05	-0.5563	-0.2959
STUDY		4	-0.2776	0.06950	15.8	-3.99	0.0011	0.05	-0.4251	-0.1301
STUDY		6	-0.2109	0.06138	12.9	-3.44	0.0045	0.05	-0.3436	-0.07816
STUDY		7	-0.1878	0.03743	32.4	-5.02	<.0001	0.05	-0.2640	-0.1116
TREAT	Drug		-0.2920	0.03253	50.8	-8.98	<.0001	0.05	-0.3573	-0.2267
TREAT	Placebo		-0.2501	0.03303	52	-7.57	<.0001	0.05	-0.3164	-0.1838
TREAT*STUDY	Drug	2	-0.3006	0.06282	66.3	-4.78	<.0001	0.05	-0.4260	-0.1752

## Meta-Analysis of Phenylephrine vs. Placebo

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Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

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The Mixed Procedure

Least Squares Means

Effect	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT*STUDY	Drug	3	-0.5931	0.08512	15.2	-6.97	<.0001	0.05	-0.7744	-0.4119
TREAT*STUDY	Drug	4	-0.2351	0.09718	15.2	-2.42	0.0285	0.05	-0.4419	-0.02820
TREAT*STUDY	Drug	6	-0.1723	0.08686	12.9	-1.98	0.0689	0.05	-0.3601	0.01546
TREAT*STUDY	Drug	7	-0.1589	0.04644	25.8	-3.42	0.0021	0.05	-0.2544	-0.06340
TREAT*STUDY	Placebo	2	-0.2052	0.06425	66.4	-3.19	0.0021	0.05	-0.3335	-0.07693
TREAT*STUDY	Placebo	3	-0.2591	0.08666	15.9	-2.99	0.0087	0.05	-0.4429	-0.07529
TREAT*STUDY	Placebo	4	-0.3201	0.09570	14.5	-3.34	0.0046	0.05	-0.5246	-0.1155
TREAT*STUDY	Placebo	6	-0.2494	0.08678	12.9	-2.87	0.0131	0.05	-0.4371	-0.06179
TREAT*STUDY	Placebo	7	-0.2167	0.05105	30.5	-4.24	0.0002	0.05	-0.3209	-0.1125

Differences of Least Squares Means

Effect	TREAT	STUDY	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
STUDY		2		3	0.1732	0.07742	28.6	2.24	0.0332	0.05	0.01480	0.3316
STUDY		2		4	0.02468	0.1058	47.9	0.23	0.8165	0.05	-0.1881	0.2374
STUDY		2		6	-0.04200	0.08902	32.5	-0.47	0.6402	0.05	-0.2232	0.1392
STUDY		2		7	-0.06508	0.08941	62.3	-0.73	0.4694	0.05	-0.2438	0.1136
STUDY		3		4	-0.1485	0.09563	33.1	-1.55	0.1299	0.05	-0.3431	0.04602
STUDY		3		6	-0.2152	0.08711	29	-2.47	0.0196	0.05	-0.3934	-0.03705
STUDY		3		7	-0.2383	0.07595	29.5	-3.14	0.0038	0.05	-0.3935	-0.08310
STUDY		4		6	-0.06668	0.09239	28.8	-0.72	0.4763	0.05	-0.2557	0.1223
STUDY		4		7	-0.08976	0.07357	19.9	-1.22	0.2367	0.05	-0.2433	0.06376
STUDY		6		7	-0.02308	0.07142	22	-0.32	0.7496	0.05	-0.1712	0.1251
TREAT	Drug		Placebo		-0.04189	0.04538	49.7	-0.92	0.3604	0.05	-0.1331	0.04927

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 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

The Mixed Procedure

Differences of Least Squares Means

Effect	TREAT	STUDY	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT*STUDY	Drug	2	Drug	3	0.2925	0.1003	23.4	2.92	0.0077	0.05	0.08528	0.4998
TREAT*STUDY	Drug	2	Drug	4	-0.06551	0.1274	33.4	-0.51	0.6104	0.05	-0.3245	0.1935
TREAT*STUDY	Drug	2	Drug	6	-0.1282	0.1093	23.8	-1.17	0.2524	0.05	-0.3540	0.09748
TREAT*STUDY	Drug	2	Drug	7	-0.1417	0.08977	55.7	-1.58	0.1202	0.05	-0.3215	0.03819
TREAT*STUDY	Drug	2	Placebo	2	-0.09537	0.01810	9.05	-5.27	0.0005	0.05	-0.1363	-0.05446
TREAT*STUDY	Drug	2	Placebo	3	-0.04148	0.09569	20.8	-0.43	0.6691	0.05	-0.2406	0.1576
TREAT*STUDY	Drug	2	Placebo	4	0.01951	0.1226	30.3	0.16	0.8746	0.05	-0.2308	0.2698
TREAT*STUDY	Drug	2	Placebo	6	-0.05113	0.1068	22.5	-0.48	0.6369	0.05	-0.2724	0.1701
TREAT*STUDY	Drug	2	Placebo	7	-0.08387	0.09905	58.2	-0.85	0.4006	0.05	-0.2821	0.1144
TREAT*STUDY	Drug	3	Drug	4	-0.3581	0.1308	30.5	-2.74	0.0102	0.05	-0.6251	-0.09106
TREAT*STUDY	Drug	3	Drug	6	-0.4208	0.1219	28.3	-3.45	0.0018	0.05	-0.6704	-0.1712
TREAT*STUDY	Drug	3	Drug	7	-0.4342	0.09847	24.5	-4.41	0.0002	0.05	-0.6372	-0.2312
TREAT*STUDY	Drug	3	Placebo	2	-0.3879	0.1011	23.8	-3.84	0.0008	0.05	-0.5966	-0.1793
TREAT*STUDY	Drug	3	Placebo	3	-0.3340	0.1200	15.1	-2.78	0.0139	0.05	-0.5898	-0.07824
TREAT*STUDY	Drug	3	Placebo	4	-0.2730	0.1292	29.5	-2.11	0.0431	0.05	-0.5371	-0.00901
TREAT*STUDY	Drug	3	Placebo	6	-0.3437	0.1215	28.1	-2.83	0.0085	0.05	-0.5925	-0.09481
TREAT*STUDY	Drug	3	Placebo	7	-0.3764	0.1017	26.3	-3.70	0.0010	0.05	-0.5853	-0.1675
TREAT*STUDY	Drug	4	Drug	6	-0.06274	0.1297	28.2	-0.48	0.6322	0.05	-0.3283	0.2028
TREAT*STUDY	Drug	4	Drug	7	-0.07615	0.1043	20	-0.73	0.4736	0.05	-0.2936	0.1413
TREAT*STUDY	Drug	4	Placebo	2	-0.02986	0.1283	34.1	-0.23	0.8174	0.05	-0.2907	0.2309
TREAT*STUDY	Drug	4	Placebo	3	0.02403	0.1335	32	0.18	0.8583	0.05	-0.2478	0.2959
TREAT*STUDY	Drug	4	Placebo	4	0.08502	0.1337	14	0.64	0.5352	0.05	-0.2018	0.3718
TREAT*STUDY	Drug	4	Placebo	6	0.01438	0.1304	28.6	0.11	0.9129	0.05	-0.2524	0.2812
TREAT*STUDY	Drug	4	Placebo	7	-0.01836	0.1041	19.9	-0.18	0.8618	0.05	-0.2355	0.1988
TREAT*STUDY	Drug	6	Drug	7	-0.01342	0.09789	20.4	-0.14	0.8923	0.05	-0.2174	0.1905
TREAT*STUDY	Drug	6	Placebo	2	0.03288	0.1102	24.3	0.30	0.7680	0.05	-0.1944	0.2602
TREAT*STUDY	Drug	6	Placebo	3	0.08676	0.1233	29	0.70	0.4871	0.05	-0.1653	0.3389

## Appendix 3

19:53 Monday, December 11, 2006 1321

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

The Mixed Procedure

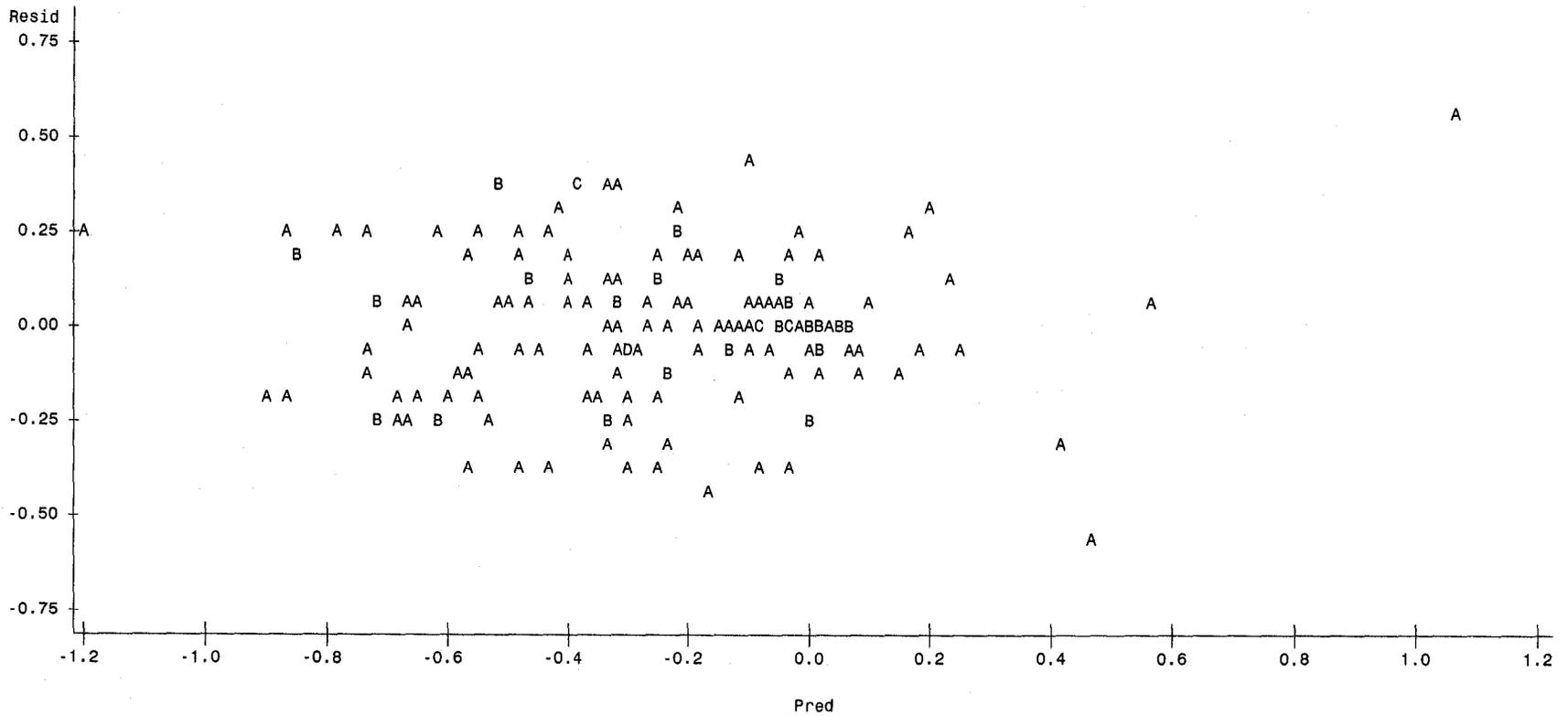
Differences of Least Squares Means

Effect	TREAT	STUDY	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT*STUDY	Drug	6	Placebo	4	0.1478	0.1288	27.8	1.15	0.2610	0.05	-0.1162	0.4117
TREAT*STUDY	Drug	6	Placebo	6	0.07712	0.1228	12.9	0.63	0.5409	0.05	-0.1884	0.3426
TREAT*STUDY	Drug	6	Placebo	7	0.04438	0.09976	21.3	0.44	0.6609	0.05	-0.1629	0.2516
TREAT*STUDY	Drug	7	Placebo	2	0.04629	0.09103	56.1	0.51	0.6131	0.05	-0.1361	0.2286
TREAT*STUDY	Drug	7	Placebo	3	0.1002	0.1013	26.1	0.99	0.3317	0.05	-0.1080	0.3084
TREAT*STUDY	Drug	7	Placebo	4	0.1612	0.1040	19.9	1.55	0.1370	0.05	-0.05588	0.3782
TREAT*STUDY	Drug	7	Placebo	6	0.09054	0.09851	20.7	0.92	0.3686	0.05	-0.1145	0.2956
TREAT*STUDY	Drug	7	Placebo	7	0.05780	0.06262	23.6	0.92	0.3654	0.05	-0.07156	0.1872
TREAT*STUDY	Placebo	2	Placebo	3	0.05389	0.09636	21.2	0.56	0.5818	0.05	-0.1464	0.2542
TREAT*STUDY	Placebo	2	Placebo	4	0.1149	0.1235	30.9	0.93	0.3596	0.05	-0.1371	0.3668
TREAT*STUDY	Placebo	2	Placebo	6	0.04425	0.1077	23	0.41	0.6849	0.05	-0.1785	0.2670
TREAT*STUDY	Placebo	2	Placebo	7	0.01151	0.1003	58.4	0.11	0.9091	0.05	-0.1893	0.2123
TREAT*STUDY	Placebo	3	Placebo	4	0.06099	0.1314	30.8	0.46	0.6457	0.05	-0.2070	0.3290
TREAT*STUDY	Placebo	3	Placebo	6	-0.00964	0.1226	28.6	-0.08	0.9378	0.05	-0.2604	0.2412
TREAT*STUDY	Placebo	3	Placebo	7	-0.04238	0.1054	28.4	-0.40	0.6906	0.05	-0.2581	0.1733
TREAT*STUDY	Placebo	4	Placebo	6	-0.07063	0.1292	28	-0.55	0.5891	0.05	-0.3354	0.1941
TREAT*STUDY	Placebo	4	Placebo	7	-0.1034	0.1046	20.2	-0.99	0.3346	0.05	-0.3214	0.1146
TREAT*STUDY	Placebo	6	Placebo	7	-0.03274	0.1008	21.9	-0.32	0.7485	0.05	-0.2419	0.1764

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
Checking the Treatment by Study Interaction Term to Test for Heterogeneity  
Patient Is Fixed  
Assuming Within Subject Variance Component Differs Across Studies  
TO = Baseline (A Covariate)

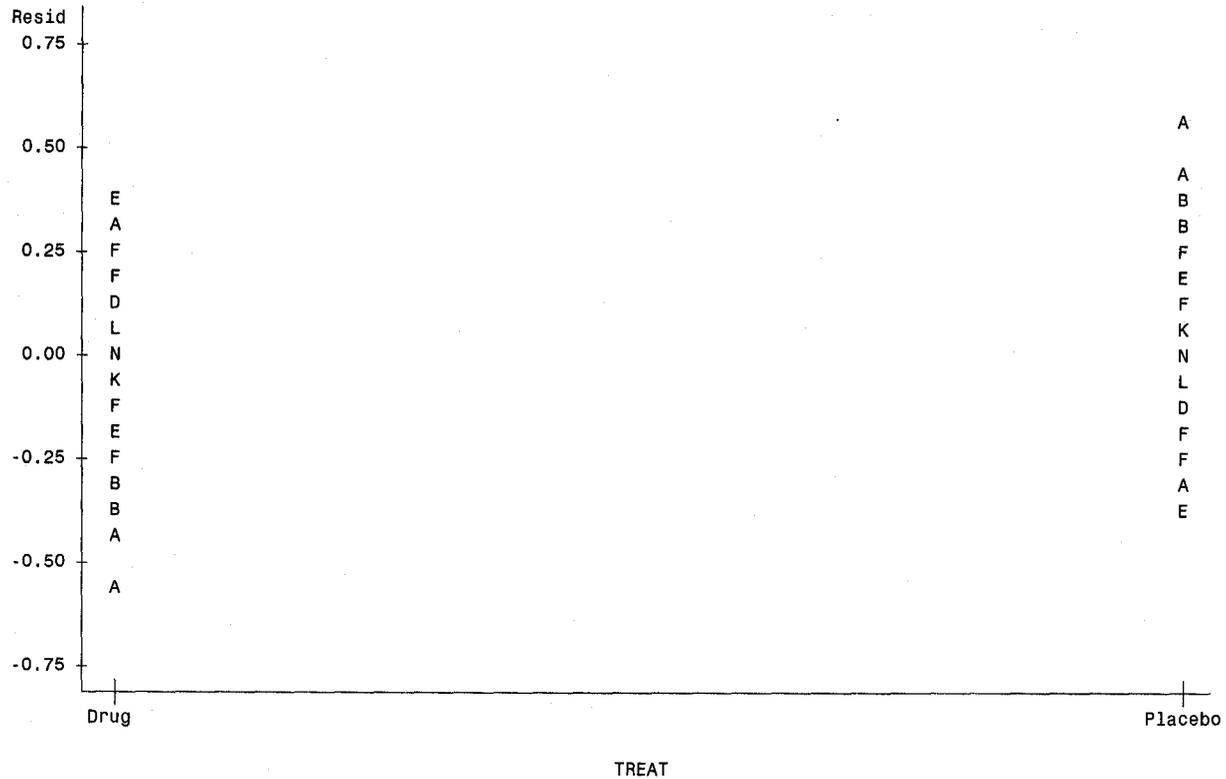
Plot of Resid\*Pred. Legend: A = 1 obs, B = 2 obs, etc.



Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
Checking the Treatment by Study Interaction Term to Test for Heterogeneity  
Patient Is Fixed  
Assuming Within Subject Variance Component Differs Across Studies  
TO = Baseline (A Covariate)

Plot of Resid\*TREAT. Legend: A = 1 obs, B = 2 obs, etc.



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Drug -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	0	Sum Observations	0
Std Deviation	0.20002604	Variance	0.04001042
Skewness	-0.1946179	Kurtosis	0.04769115
Uncorrected SS	3.24084387	Corrected SS	3.24084387
Coeff Variation	.	Std Error Mean	0.02208918

## Basic Statistical Measures

Location		Variability	
Mean	0.00000	Std Deviation	0.20003
Median	-0.00209	Variance	0.04001
Mode	.	Range	0.95712
		Interquartile Range	0.23273

## Tests for Location: Mu0=0

Test	-Statistic-		-----p Value-----
Student's t	t	0	Pr >  t  1.0000
Sign	M	0	Pr >=  M  1.0000
Signed Rank	S	31.5	Pr >=  S  0.8853

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity  
 Patient Is Fixed  
 Assuming Within Subject Variance Component Differs Across Studies  
 TO = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure  
 Variable: Resid

## Tests for Normality

Test	--Statistic---	-----p Value-----
Shapiro-Wilk	W 0.986957	Pr < W 0.5786
Kolmogorov-Smirnov	D 0.072809	Pr > D >0.1500
Cramer-von Mises	W-Sq 0.051779	Pr > W-Sq >0.2500
Anderson-Darling	A-Sq 0.297332	Pr > A-Sq >0.2500

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	0.39566870
99%	0.39566870
95%	0.35022044
90%	0.27966407
75% Q3	0.10520152
50% Median	-0.00209164
25% Q1	-0.12753259
10%	-0.26044897
5%	-0.30550914
1%	-0.56145522
0% Min	-0.56145522

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.561455	6026	24	0.350220	3044	80
-0.468280	3026	75	0.355076	3046	81
-0.373199	4010	4	0.378800	4003	2
-0.362850	4001	1	0.388270	4017	6
-0.305509	4012	5	0.395669	7034	60



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)

Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	0	Sum Observations	0
Std Deviation	0.20002604	Variance	0.04001042
Skewness	0.19461788	Kurtosis	0.04769115
Uncorrected SS	3.24084387	Corrected SS	3.24084387
Coeff Variation	.	Std Error Mean	0.02208918

## Basic Statistical Measures

Location		Variability	
Mean	0.000000	Std Deviation	0.20003
Median	0.002092	Variance	0.04001
Mode	.	Range	0.95712
		Interquartile Range	0.23273

## Tests for Location: MU0=0

Test	-Statistic-		-----p Value-----	
Student's t	t	0	Pr >  t	1.0000
Sign	M	0	Pr >=  M	1.0000
Signed Rank	S	-31.5	Pr >=  S	0.8853

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

## Tests for Normality

Test	--Statistic--	-----p Value-----
Shapiro-Wilk	W 0.986957	Pr < W 0.5786
Kolmogorov-Smirnov	D 0.072809	Pr > D >0.1500
Cramer-von Mises	W-Sq 0.051779	Pr > W-Sq >0.2500
Anderson-Darling	A-Sq 0.297332	Pr > A-Sq >0.2500

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	0.56145522
99%	0.56145522
95%	0.30550914
90%	0.26044897
75% Q3	0.12753259
50% Median	0.00209164
25% Q1	-0.10520152
10%	-0.27966407
5%	-0.35022044
1%	-0.39566870
0% Min	-0.39566870

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

## Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.395669	7034	60	0.305509	4012	5
-0.388270	4017	6	0.362850	4001	1
-0.378800	4003	2	0.373199	4010	4
-0.355076	3046	81	0.468280	3026	75
-0.350220	3044	80	0.561455	6026	24



Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Fixed

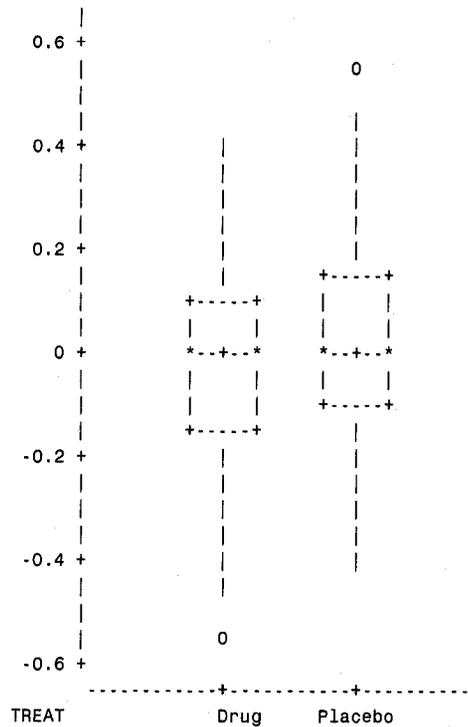
Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

The UNIVARIATE Procedure

Variable: Resid

Schematic Plots



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

The Mixed Procedure

## Model Information

Data Set	WORK.TEN_MG
Dependent Variable	LN180CHG
Covariance Structure	Variance Components
Group Effect	STUDY
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Prasad-Rao-Jeske- Kackar-Harville
Degrees of Freedom Method	Kenward-Roger

## Class Level Information

Class	Levels	Values
STUDY	5	2 3 4 6 7
TREAT	2	Drug Placebo
PATIENT	82	2001 2005 2007 2012 2014 2018 2020 2021 2023 2024 3001 3003 3005 3008 3009 3015 3018 3023 3026 3032 3036 3039 3041 3044 3046 3048 4001 4003 4007 4010 4012 4017 4024 4026 4027 4030 4032 4034 4037 4039 4044 6001 6003 6005 6008 6010 6013 6017 6023 6026 6031 6034 6040 6041 6044 6046 6048 7001 7002 7003 7007 7008 7010 7014 7016 7017 7018 7020 7021 7025 7027 7028 7030 7031 7033 7034 7036 7041 7042 7044 7048 7050

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

## The Mixed Procedure

## Dimensions

Covariance Parameters	5
Columns in X	91
Columns in Z	0
Subjects	164
Max Obs Per Subject	1
Observations Used	164
Observations Not Used	0
Total Observations	164

## Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	105.65612721	
1	2	72.22574019	0.00621893
2	1	72.01462049	0.00028740
3	1	72.00344916	0.00000111
4	1	72.00340731	0.00000000

Convergence criteria met.

## Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	STUDY 2	0.001715
Residual	STUDY 3	0.1396
Residual	STUDY 4	0.1416

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

## The Mixed Procedure

## Covariance Parameter Estimates

Cov Parm	Group	Estimate
Residual	STUDY 6	0.1182
Residual	STUDY 7	0.05667

## Fit Statistics

-2 Res Log Likelihood	72.0
AIC (smaller is better)	82.0
AICC (smaller is better)	82.8
BIC (smaller is better)	97.5

## Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
4	33.65	<.0001

## Type 3 Tests of Fixed Effects

Effect	Num	Den	F Value	Pr > F
	DF	DF		
TO	1	71.1	14.30	0.0003
PATIENT(STUDY)	77	28.4	2.05	0.0171
STUDY	4	37.9	2.58	0.0529
TREAT	1	10.9	20.85	0.0008

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

## The Mixed Procedure

## Least Squares Means

Effect	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	-0.3158	0.02616	64.3	-12.07	<.0001	0.05	-0.3680	-0.2635
TREAT	Placebo	-0.2334	0.02642	66.2	-8.83	<.0001	0.05	-0.2861	-0.1806

## Differences of Least Squares Means

Effect	TREAT	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	Placebo	-0.08241	0.01805	10.9	-4.57	0.0008	0.05	-0.1222	-0.04266

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

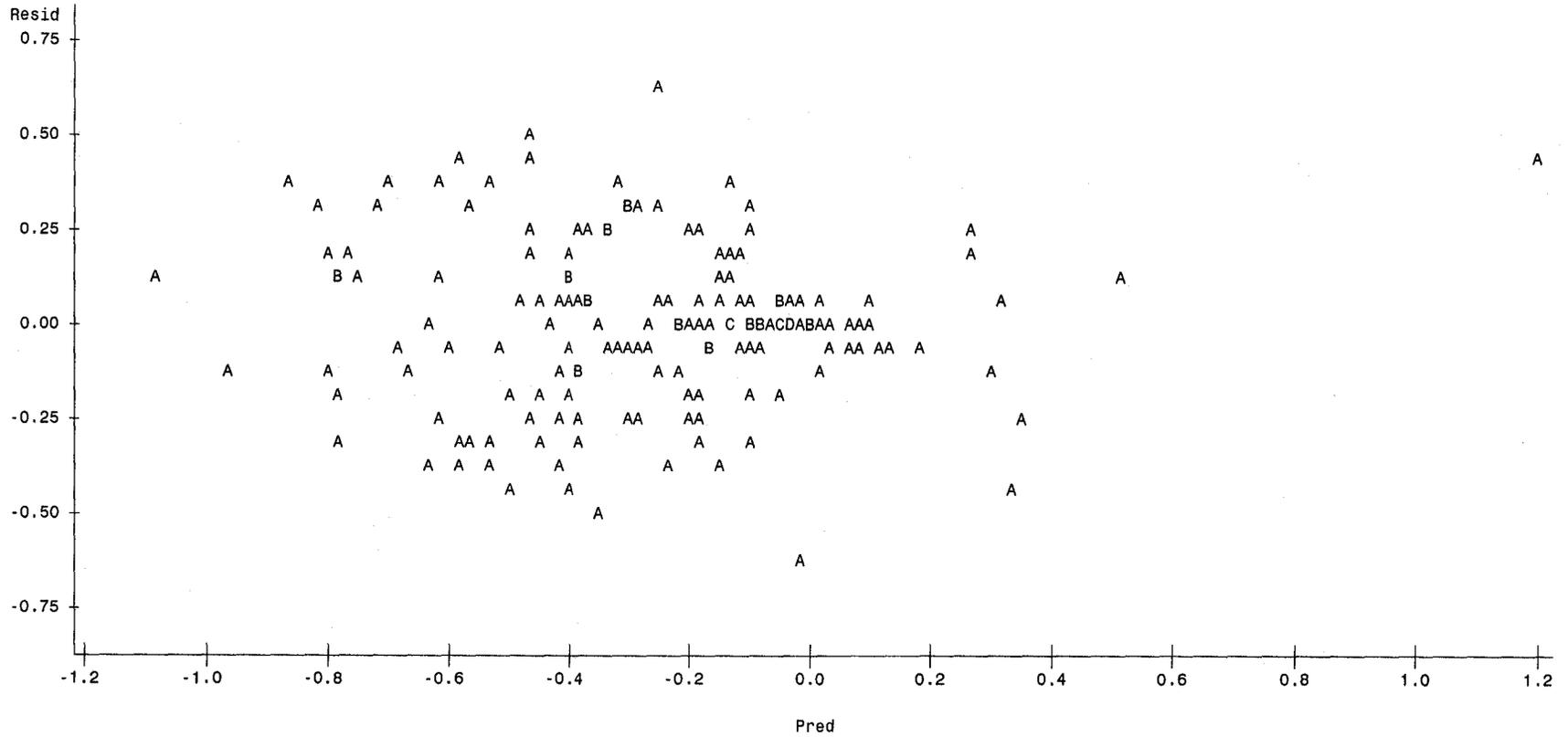
Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

Plot of Resid\*Pred. Legend: A = 1 obs, B = 2 obs, etc.



Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

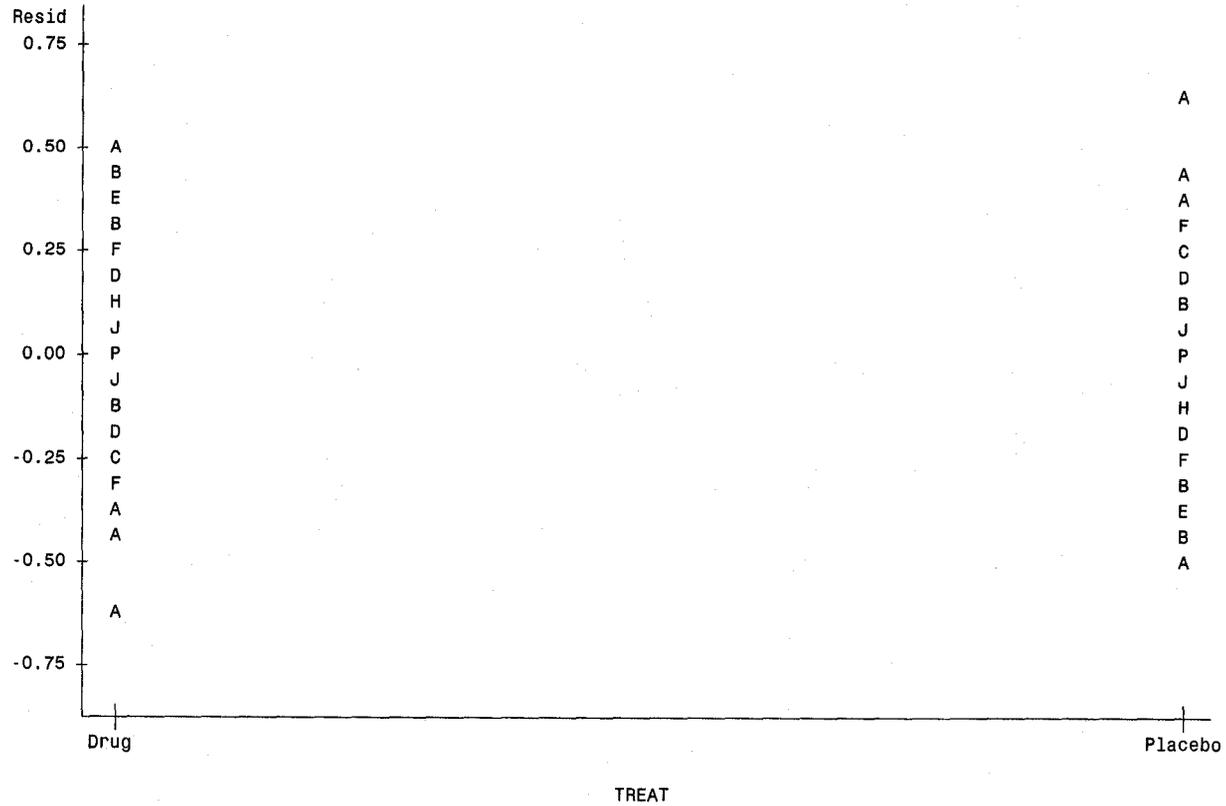
Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

Plot of Resid\*TREAT. Legend: A = 1 obs, B = 2 obs, etc.



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure  
Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	0.027163	Sum Observations	2.22736616
Std Deviation	0.21468647	Variance	0.04609028
Skewness	-0.2096151	Kurtosis	0.27385263
Uncorrected SS	3.79381479	Corrected SS	3.73331284
Coeff Variation	790.363577	Std Error Mean	0.02370815

## Basic Statistical Measures

Location		Variability	
Mean	0.027163	Std Deviation	0.21469
Median	0.020917	Variance	0.04609
Mode	.	Range	1.08845
		Interquartile Range	0.21955

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----
Student's t	t 1.145724	Pr >  t  0.2553
Sign	M 5	Pr >=  M  0.3203
Signed Rank	S 274.5	Pr >=  S  0.2064

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

## Tests for Normality

Test	--Statistic--	-----p Value-----
Shapiro-Wilk	W 0.98324	Pr < W 0.3624
Kolmogorov-Smirnov	D 0.090365	Pr > D 0.0955
Cramer-von Mises	W-Sq 0.095191	Pr > W-Sq 0.1316
Anderson-Darling	A-Sq 0.502233	Pr > A-Sq 0.2093

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	0.4743062
99%	0.4743062
95%	0.3774318
90%	0.3152541
75% Q3	0.1543923
50% Median	0.0209172
25% Q1	-0.0651573
10%	-0.2893421
5%	-0.3060348
1%	-0.6141473
0% Min	-0.6141473

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.614147	3026	75	0.377432	6046	30
-0.430686	6026	24	0.377508	4007	3
-0.381164	3039	78	0.460622	4003	2
-0.316808	3003	68	0.465625	7034	60
-0.306035	3008	70	0.474306	4017	6



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	-0.027163	Sum Observations	-2.2273662
Std Deviation	0.21468647	Variance	0.04609028
Skewness	0.20961514	Kurtosis	0.27385263
Uncorrected SS	3.79381479	Corrected SS	3.73331284
Coeff Variation	-790.36358	Std Error Mean	0.02370815

## Basic Statistical Measures

Location		Variability	
Mean	-0.02716	Std Deviation	0.21469
Median	-0.02092	Variance	0.04609
Mode	.	Range	1.08845
		Interquartile Range	0.21955

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----
Student's t	t -1.14572	Pr >  t  0.2553
Sign	M -5	Pr >=  M  0.3203
Signed Rank	S -274.5	Pr >=  S  0.2064

Appendix 3

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

Tests for Normality

Test	--Statistic--	-----p Value-----
Shapiro-Wilk	W 0.98324	Pr < W 0.3624
Kolmogorov-Smirnov	D 0.090365	Pr > D 0.0955
Cramer-von Mises	W-Sq 0.095191	Pr > W-Sq 0.1316
Anderson-Darling	A-Sq 0.502233	Pr > A-Sq 0.2093

Quantiles (Definition 5)

Quantile	Estimate
100% Max	0.6141473
99%	0.6141473
95%	0.3060348
90%	0.2893421
75% Q3	0.0651573
50% Median	-0.0209172
25% Q1	-0.1543923
10%	-0.3152541
5%	-0.3774318
1%	-0.4743062
0% Min	-0.4743062

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

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Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

## Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.474306	4017	6	0.306035	3008	70
-0.465625	7034	60	0.316808	3003	68
-0.460622	4003	2	0.381164	3039	78
-0.377508	4007	3	0.430686	6026	24
-0.377432	6046	30	0.614147	3026	75

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes  
 Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

Assuming Within Subject Variance Component Differs Across Studies

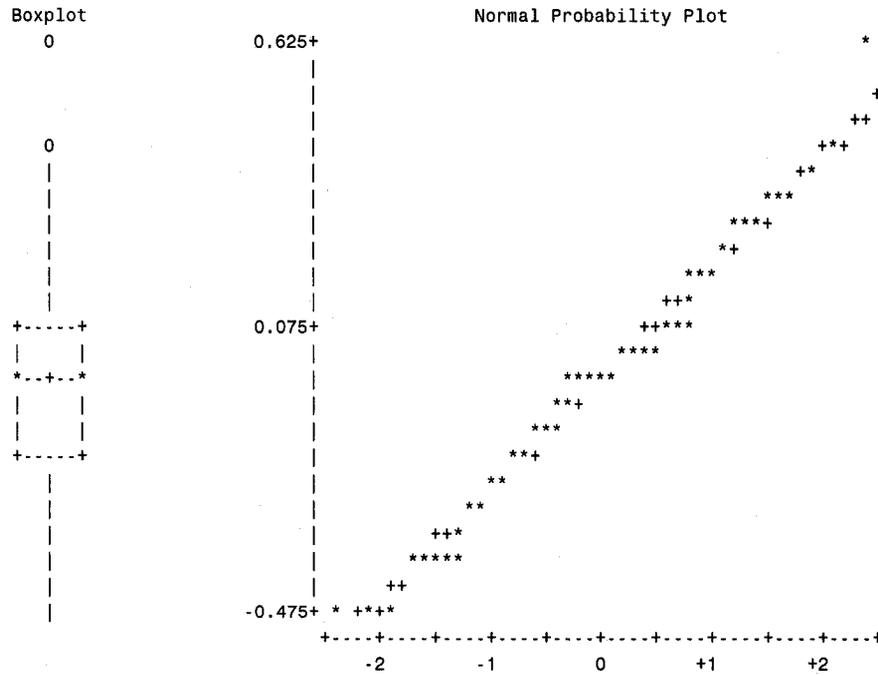
T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure  
 Variable: Resid

Stem Leaf	#
6 1	1
5	
5	
4	
4 3	1
3 8	1
3 0012	4
2 599	3
2 22	2
1 56899	5
1 0	1
0 5556788	7
0 01122223344	11
-0 4432222110	11
-0 9999555	7
-1 444210	6
-1 98755	5
-2 44220	5
-2 977	3
-3 2	1
-3 88666	5
-4	
-4 776	3

-----+-----+-----+  
 Multiply Stem.Leaf by 10\*\*-1



Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 180 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Fixed

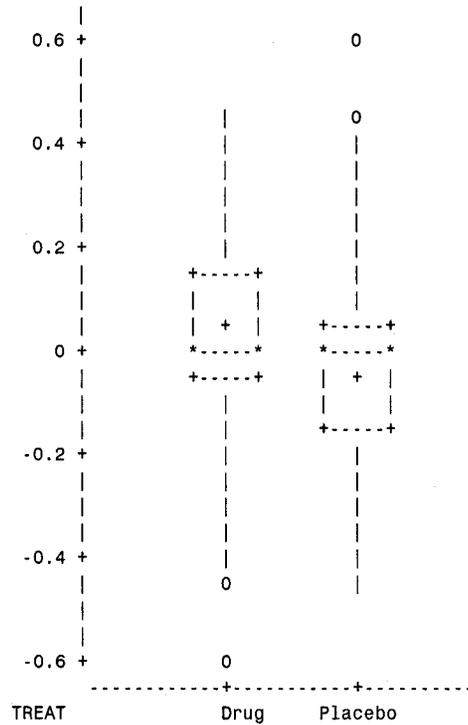
Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

The UNIVARIATE Procedure

Variable: Resid

Schematic Plots



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

The Mixed Procedure

## Model Information

Data Set	WORK.TEN_MG
Dependent Variable	LN240CHG
Covariance Structure	Variance Components
Subject Effect	PATIENT(STUDY)
Group Effects	STUDY, STUDY
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Prasad-Rao-Jeske- Kackar-Harville
Degrees of Freedom Method	Kenward-Roger

## Class Level Information

Class	Levels	Values
TREAT	2	Drug Placebo
STUDY	5	2 3 4 6 7

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
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Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

## The Mixed Procedure

## Class Level Information

Class	Levels	Values
PATIENT	82	2001 2005 2007 2012 2014 2018 2020 2021 2023 2024 3001 3003 3005 3008 3009 3015 3018 3023 3026 3032 3036 3039 3041 3044 3046 3048 4001 4003 4007 4010 4012 4017 4024 4026 4027 4030 4032 4034 4037 4039 4044 6001 6003 6005 6008 6010 6013 6017 6023 6026 6031 6034 6040 6041 6044 6046 6048 7001 7002 7003 7007 7008 7010 7014 7016 7017 7018 7020 7021 7025 7027 7028 7030 7031 7033 7034 7036 7041 7042 7044 7048 7050

## Dimensions

Covariance Parameters	10
Columns in X	19
Columns in Z Per Subject	5
Subjects	82
Max Obs Per Subject	2
Observations Used	164
Observations Not Used	0
Total Observations	164

Appendix 3

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
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Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	203.47521515	
1	4	140.79446900	0.00076122
2	1	140.74497857	0.00000798
3	1	140.74441410	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
Intercept	PATIENT(STUDY)	STUDY 2	0
Intercept	PATIENT(STUDY)	STUDY 3	0.04763
Intercept	PATIENT(STUDY)	STUDY 4	0
Intercept	PATIENT(STUDY)	STUDY 6	0.06309
Intercept	PATIENT(STUDY)	STUDY 7	0.04310
Residual		STUDY 2	0.003349
Residual		STUDY 3	0.1809
Residual		STUDY 4	0.1766
Residual		STUDY 6	0.2055
Residual		STUDY 7	0.09855

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

## The Mixed Procedure

## Fit Statistics

-2 Res Log Likelihood	140.7
AIC (smaller is better)	156.7
AICC (smaller is better)	157.7
BIC (smaller is better)	176.0

## Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
TO	1	82.7	7.06	0.0094
STUDY	4	40.6	2.74	0.0413
TREAT	1	60.6	0.70	0.4056
TREAT*STUDY	4	36.6	1.56	0.2069

## Least Squares Means

Effect	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
STUDY		2	-0.1162	0.03980	90.2	-2.92	0.0044	0.05	-0.1952	-0.03711
STUDY		3	-0.2542	0.09328	15	-2.73	0.0156	0.05	-0.4531	-0.05540
STUDY		4	-0.4019	0.07761	28.8	-5.18	<.0001	0.05	-0.5607	-0.2431
STUDY		6	-0.08241	0.1018	14.9	-0.81	0.4310	0.05	-0.2995	0.1347
STUDY		7	-0.2044	0.06212	22.1	-3.29	0.0033	0.05	-0.3332	-0.07556
TREAT	Drug		-0.2356	0.04433	105	-5.31	<.0001	0.05	-0.3235	-0.1477
TREAT	Placebo		-0.1881	0.04446	105	-4.23	<.0001	0.05	-0.2762	-0.09990
TREAT*STUDY	Drug	2	-0.1284	0.04145	86.6	-3.10	0.0026	0.05	-0.2108	-0.04604

Appendix 3

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)

Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

The Mixed Procedure

Least Squares Means

Effect	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT*STUDY	Drug	3	-0.4424	0.1196	27.8	-3.70	0.0009	0.05	-0.6875	-0.1972
TREAT*STUDY	Drug	4	-0.3674	0.1094	28.5	-3.36	0.0022	0.05	-0.5913	-0.1435
TREAT*STUDY	Drug	6	-0.05252	0.1296	28.3	-0.41	0.6883	0.05	-0.3178	0.2128
TREAT*STUDY	Drug	7	-0.1872	0.07588	41.4	-2.47	0.0179	0.05	-0.3404	-0.03399
TREAT*STUDY	Placebo	2	-0.1039	0.04225	87.2	-2.46	0.0159	0.05	-0.1879	-0.01994
TREAT*STUDY	Placebo	3	-0.06612	0.1200	28.1	-0.55	0.5861	0.05	-0.3120	0.1797
TREAT*STUDY	Placebo	4	-0.4364	0.1089	28.2	-4.01	0.0004	0.05	-0.6595	-0.2134
TREAT*STUDY	Placebo	6	-0.1123	0.1296	28.2	-0.87	0.3933	0.05	-0.3776	0.1530
TREAT*STUDY	Placebo	7	-0.2216	0.07696	42.2	-2.88	0.0062	0.05	-0.3768	-0.06628

Differences of Least Squares Means

Effect	TREAT	STUDY	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
STUDY		2		3	0.1381	0.09823	17.9	1.41	0.1770	0.05	-0.06842	0.3446
STUDY		2		4	0.2857	0.09213	45.8	3.10	0.0033	0.05	0.1003	0.4712
STUDY		2		6	-0.03376	0.1097	18.9	-0.31	0.7616	0.05	-0.2633	0.1958
STUDY		2		7	0.08821	0.08005	34.8	1.10	0.2780	0.05	-0.07433	0.2507
STUDY		3		4	0.1476	0.1222	35.1	1.21	0.2348	0.05	-0.1003	0.3956
STUDY		3		6	-0.1718	0.1381	29.9	-1.24	0.2232	0.05	-0.4540	0.1103
STUDY		3		7	-0.04986	0.1130	28.7	-0.44	0.6624	0.05	-0.2811	0.1814
STUDY		4		6	-0.3195	0.1279	31.5	-2.50	0.0179	0.05	-0.5802	-0.05873
STUDY		4		7	-0.1975	0.09789	47.5	-2.02	0.0493	0.05	-0.3944	-0.00064
STUDY		6		7	0.1220	0.1192	25.2	1.02	0.3158	0.05	-0.1233	0.3673
TREAT	Drug		Placebo		-0.04751	0.05673	60.6	-0.84	0.4056	0.05	-0.1610	0.06594

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
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Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

The Mixed Procedure

Differences of Least Squares Means

Effect	TREAT	STUDY	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT*STUDY	Drug	2	Drug	3	0.3139	0.1250	32.2	2.51	0.0172	0.05	0.05945	0.5684
TREAT*STUDY	Drug	2	Drug	4	0.2389	0.1213	38.4	1.97	0.0562	0.05	-0.00660	0.4845
TREAT*STUDY	Drug	2	Drug	6	-0.07592	0.1367	33.4	-0.56	0.5823	0.05	-0.3538	0.2020
TREAT*STUDY	Drug	2	Drug	7	0.05876	0.09051	53.8	0.65	0.5190	0.05	-0.1227	0.2402
TREAT*STUDY	Drug	2	Placebo	2	-0.02453	0.02589	17.9	-0.95	0.3561	0.05	-0.07896	0.02990
TREAT*STUDY	Drug	2	Placebo	3	-0.06232	0.1236	31.2	-0.50	0.6178	0.05	-0.3144	0.1898
TREAT*STUDY	Drug	2	Placebo	4	0.3080	0.1195	36.9	2.58	0.0141	0.05	0.06580	0.5502
TREAT*STUDY	Drug	2	Placebo	6	-0.01612	0.1359	32.9	-0.12	0.9063	0.05	-0.2927	0.2605
TREAT*STUDY	Drug	2	Placebo	7	0.09313	0.09398	55.7	0.99	0.3260	0.05	-0.09516	0.2814
TREAT*STUDY	Drug	3	Drug	4	-0.07500	0.1626	56.7	-0.46	0.6463	0.05	-0.4006	0.2506
TREAT*STUDY	Drug	3	Drug	6	-0.3898	0.1764	55	-2.21	0.0313	0.05	-0.7434	-0.03626
TREAT*STUDY	Drug	3	Drug	7	-0.2552	0.1421	50.9	-1.80	0.0784	0.05	-0.5404	0.03003
TREAT*STUDY	Drug	3	Placebo	2	-0.3385	0.1252	32.4	-2.70	0.0108	0.05	-0.5933	-0.08357
TREAT*STUDY	Drug	3	Placebo	3	-0.3762	0.1505	14.6	-2.50	0.0248	0.05	-0.6977	-0.05480
TREAT*STUDY	Drug	3	Placebo	4	-0.00594	0.1621	56.3	-0.04	0.9709	0.05	-0.3307	0.3188
TREAT*STUDY	Drug	3	Placebo	6	-0.3301	0.1763	54.9	-1.87	0.0666	0.05	-0.6835	0.02335
TREAT*STUDY	Drug	3	Placebo	7	-0.2208	0.1429	51.6	-1.55	0.1284	0.05	-0.5076	0.06596
TREAT*STUDY	Drug	4	Drug	6	-0.3148	0.1694	55.1	-1.86	0.0684	0.05	-0.6543	0.02462
TREAT*STUDY	Drug	4	Drug	7	-0.1802	0.1321	52.2	-1.36	0.1785	0.05	-0.4453	0.08494
TREAT*STUDY	Drug	4	Placebo	2	-0.2635	0.1217	38.7	-2.16	0.0366	0.05	-0.5097	-0.01723
TREAT*STUDY	Drug	4	Placebo	3	-0.3012	0.1634	57.4	-1.84	0.0704	0.05	-0.6283	0.02586
TREAT*STUDY	Drug	4	Placebo	4	0.06906	0.1535	27.9	0.45	0.6563	0.05	-0.2454	0.3836
TREAT*STUDY	Drug	4	Placebo	6	-0.2550	0.1696	55.3	-1.50	0.1383	0.05	-0.5949	0.08479
TREAT*STUDY	Drug	4	Placebo	7	-0.1458	0.1321	52.2	-1.10	0.2747	0.05	-0.4108	0.1192
TREAT*STUDY	Drug	6	Drug	7	0.1347	0.1500	47.4	0.90	0.3739	0.05	-0.1671	0.4364
TREAT*STUDY	Drug	6	Placebo	2	0.05139	0.1369	33.6	0.38	0.7098	0.05	-0.2270	0.3298
TREAT*STUDY	Drug	6	Placebo	3	0.01360	0.1768	55.3	0.08	0.9389	0.05	-0.3406	0.3678

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
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Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

The Mixed Procedure

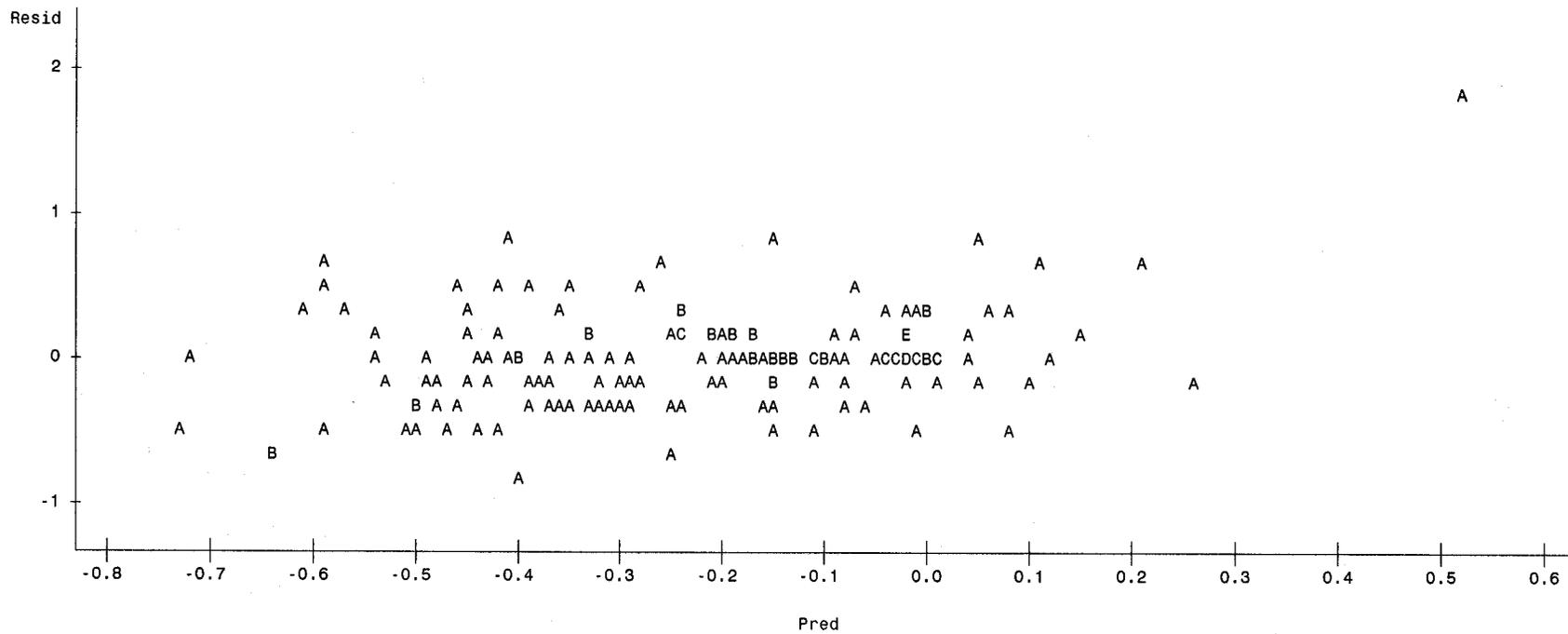
Differences of Least Squares Means

Effect	TREAT	STUDY	TREAT	STUDY	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT*STUDY	Drug	6	Placebo	4	0.3839	0.1691	54.9	2.27	0.0272	0.05	0.04491	0.7229
TREAT*STUDY	Drug	6	Placebo	6	0.05980	0.1603	14.2	0.37	0.7146	0.05	-0.2836	0.4032
TREAT*STUDY	Drug	6	Placebo	7	0.1690	0.1505	47.7	1.12	0.2669	0.05	-0.1335	0.4716
TREAT*STUDY	Drug	7	Placebo	2	-0.08329	0.09097	54	-0.92	0.3639	0.05	-0.2657	0.09908
TREAT*STUDY	Drug	7	Placebo	3	-0.1211	0.1428	51.5	-0.85	0.4004	0.05	-0.4076	0.1655
TREAT*STUDY	Drug	7	Placebo	4	0.2492	0.1321	52.2	1.89	0.0647	0.05	-0.01574	0.5142
TREAT*STUDY	Drug	7	Placebo	6	-0.07488	0.1502	47.5	-0.50	0.6203	0.05	-0.3769	0.2271
TREAT*STUDY	Drug	7	Placebo	7	0.03437	0.08902	23.8	0.39	0.7029	0.05	-0.1494	0.2182
TREAT*STUDY	Placebo	2	Placebo	3	-0.03778	0.1238	31.3	-0.31	0.7623	0.05	-0.2902	0.2147
TREAT*STUDY	Placebo	2	Placebo	4	0.3325	0.1199	37.2	2.77	0.0086	0.05	0.08969	0.5753
TREAT*STUDY	Placebo	2	Placebo	6	0.008408	0.1362	33.1	0.06	0.9511	0.05	-0.2686	0.2855
TREAT*STUDY	Placebo	2	Placebo	7	0.1177	0.09448	55.9	1.25	0.2182	0.05	-0.07162	0.3069
TREAT*STUDY	Placebo	3	Placebo	4	0.3703	0.1627	56.9	2.28	0.0267	0.05	0.04439	0.6962
TREAT*STUDY	Placebo	3	Placebo	6	0.04619	0.1766	55.2	0.26	0.7946	0.05	-0.3077	0.4001
TREAT*STUDY	Placebo	3	Placebo	7	0.1554	0.1439	52.4	1.08	0.2848	0.05	-0.1332	0.4441
TREAT*STUDY	Placebo	4	Placebo	6	-0.3241	0.1693	55	-1.91	0.0607	0.05	-0.6633	0.01513
TREAT*STUDY	Placebo	4	Placebo	7	-0.2149	0.1322	52.3	-1.63	0.1102	0.05	-0.4801	0.05042
TREAT*STUDY	Placebo	6	Placebo	7	0.1092	0.1507	47.9	0.72	0.4721	0.05	-0.1938	0.4123

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
Checking the Treatment by Study Interaction Term to Test for Heterogeneity  
Patient Is Random  
Assuming Within Subject Variance Component Differs Across Studies  
TO = Baseline (A Covariate)

Plot of Resid\*Pred. Legend: A = 1 obs, B = 2 obs, etc.



Meta-Analysis of Phenylephrine vs. Placebo

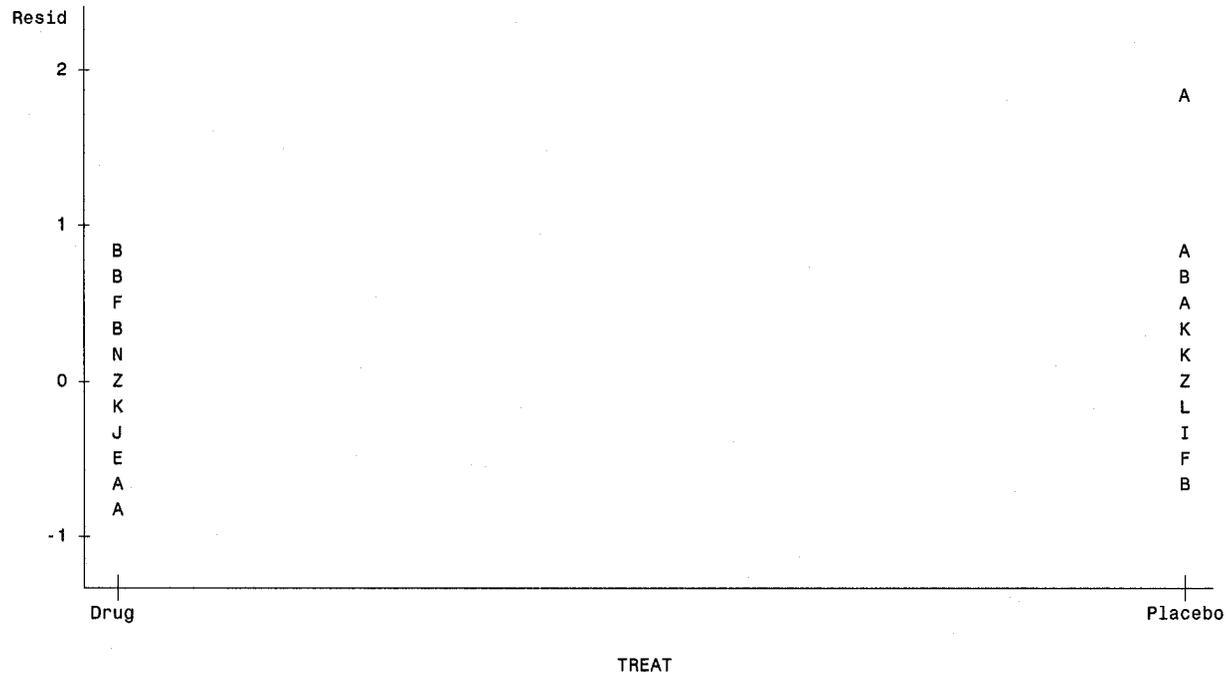
Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

Plot of Resid\*TREAT. Legend: A = 1 obs, B = 2 obs, etc.



NOTE: 2 obs hidden.

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	0	Sum Observations	0
Std Deviation	0.31668299	Variance	0.10028811
Skewness	0.34018721	Kurtosis	0.61418607
Uncorrected SS	8.12333723	Corrected SS	8.12333723
Coeff Variation	.	Std Error Mean	0.03497179

## Basic Statistical Measures

Location		Variability	
Mean	0.00000	Std Deviation	0.31668
Median	-0.00898	Variance	0.10029
Mode	.	Range	1.67663
		Interquartile Range	0.31580

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----
Student's t	t      0	Pr >  t     1.0000
Sign	M      -3	Pr >=  M    0.5811
Signed Rank	S     -81.5	Pr >=  S    0.7088

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

Tests for Normality

Test	--Statistic--	-----p Value-----
Shapiro-Wilk	W 0.973841	Pr < W 0.0920
Kolmogorov-Smirnov	D 0.100094	Pr > D 0.0418
Cramer-von Mises	W-Sq 0.179577	Pr > W-Sq 0.0094
Anderson-Darling	A-Sq 0.952675	Pr > A-Sq 0.0168

Quantiles (Definition 5)

Quantile	Estimate
100% Max	0.86848103
99%	0.86848103
95%	0.57783692
90%	0.47818720
75% Q3	0.15779770
50% Median	-0.00897974
25% Q1	-0.15800619
10%	-0.36970627
5%	-0.49522454
1%	-0.80815001
0% Min	-0.80815001

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.808150	4010	4	0.577837	4017	6
-0.594165	3005	69	0.596641	6005	18
-0.579084	3001	67	0.671468	3046	81
-0.552556	3015	72	0.804399	7018	51
-0.495225	7002	43	0.868481	3026	75

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

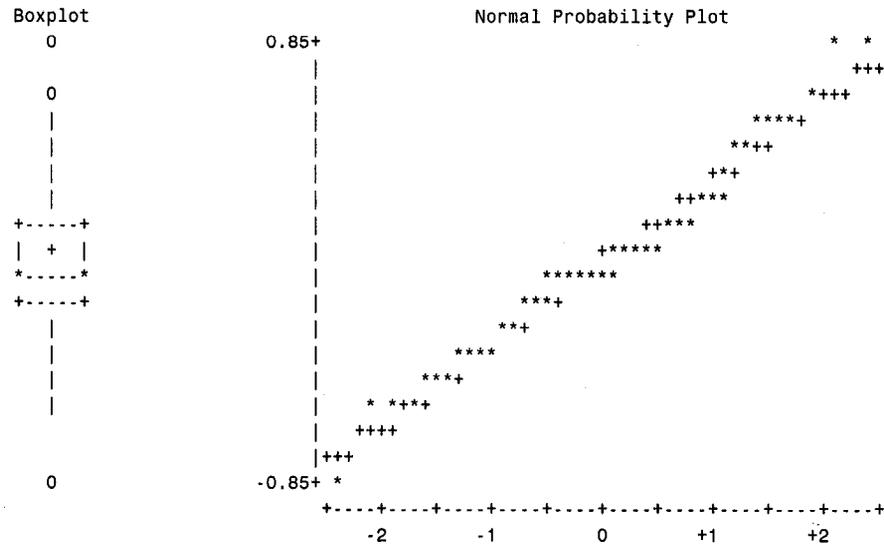
T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure  
 Variable: Resid

Stem Leaf	#
8 07	2
7	
6 07	2
5 258	3
4 689	3
3 01	2
2 02234	5
1 3456889	7
0 00112233457799	14
-0 998887764432221100	18
-1 6653321	7
-2 88750	5
-3 8776321	7
-4 73	2
-5 9850	4
-6	
-7	
-8 1	1

-----+-----+-----+-----+  
 Multiply Stem.Leaf by 10\*\*-1



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	0	Sum Observations	0
Std Deviation	0.34951563	Variance	0.12216117
Skewness	1.64663292	Kurtosis	7.98275206
Uncorrected SS	9.89505505	Corrected SS	9.89505505
Coeff Variation	.	Std Error Mean	0.03859754

## Basic Statistical Measures

Location		Variability	
Mean	0.00000	Std Deviation	0.34952
Median	-0.01431	Variance	0.12216
Mode	.	Range	2.54792
		Interquartile Range	0.32216

## Tests for Location: Mu0=0

Test	-Statistic-	-p Value-----
Student's t	t 0	Pr >  t  1.0000
Sign	M -2	Pr >=  M  0.7407
Signed Rank	S -95.5	Pr >=  S  0.6616

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

Tests for Normality

Test	--Statistic---	-----p Value-----
Shapiro-Wilk	W 0.887022	Pr < W <0.0001
Kolmogorov-Smirnov	D 0.100139	Pr > D 0.0416
Cramer-von Mises	W-Sq 0.240951	Pr > W-Sq <0.0050
Anderson-Darling	A-Sq 1.45698	Pr > A-Sq <0.0050

Quantiles (Definition 5)

Quantile	Estimate
100% Max	1.8041424
99%	1.8041424
95%	0.4539321
90%	0.3003857
75% Q3	0.1531664
50% Median	-0.0143142
25% Q1	-0.1689980
10%	-0.4148030
5%	-0.5009657
1%	-0.7437732
0% Min	-0.7437732

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random

Assuming Within Subject Variance Component Differs Across Studies

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.743773	4017	6	0.453932	4010	4
-0.592585	6041	28	0.583980	3023	74
-0.569199	6005	18	0.632148	4001	1
-0.555865	4003	2	0.830639	4037	13
-0.500966	7021	53	1.804142	6026	24

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction)  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity  
 Patient Is Random  
 Assuming Within Subject Variance Component Differs Across Studies  
 T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure  
 Variable: Resid

Stem Leaf	#
18 0	1
16	
14	
12	
10	
8 3	1
6 3	1
4 158	3
2 5666778056	10
0 0222345555799024557899	23
-0 877765320098755433322211	25
-2 88209952	8
-4 976083211	9
-6 4	1

-----+-----+-----+-----+  
 Multiply Stem.Leaf by 10\*\*-1

Boxplot

\*

0

+---+---+

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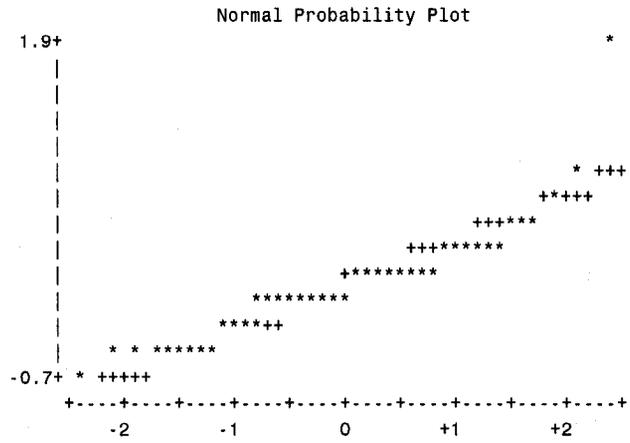
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0



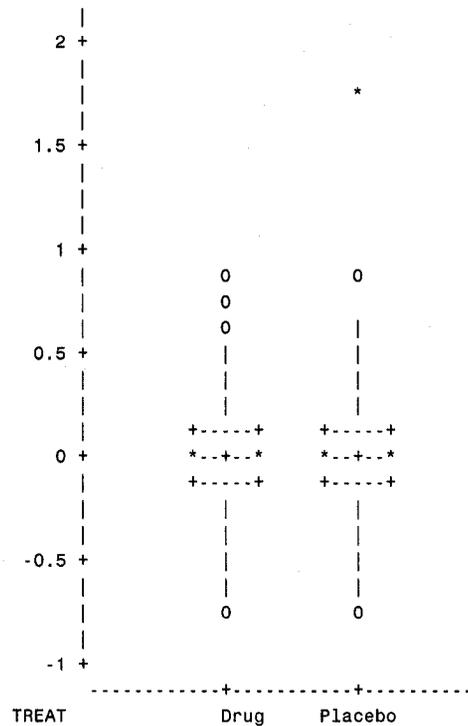
Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 1: Fixed Effects Model to Test Heterogeneity, Adjusting for Baseline NAR (Nasal Airflow Resistance and Study with Treatment by Study Interaction  
 Checking the Treatment by Study Interaction Term to Test for Heterogeneity

Patient Is Random  
 Assuming Within Subject Variance Component Differs Across Studies  
 T0 = Baseline (A Covariate)

The UNIVARIATE Procedure  
 Variable: Resid

Schematic Plots



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

TO = Baseline (A Covariate)

The Mixed Procedure

## Model Information

Data Set	WORK.TEN_MG
Dependent Variable	LN240CHG
Covariance Structure	Compound Symmetry
Subject Effect	PATIENT(STUDY)
Group Effect	STUDY
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Prasad-Rao-Jeske- Kacker-Harville
Degrees of Freedom Method	Kenward-Roger

## Class Level Information

Class	Levels	Values
STUDY	5	2 3 4 6 7
TREAT	2	Drug Placebo

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

The Mixed Procedure

## Class Level Information

Class	Levels	Values
PATIENT	82	2001 2005 2007 2012 2014 2018 2020 2021 2023 2024 3001 3003 3005 3008 3009 3015 3018 3023 3026 3032 3036 3039 3041 3044 3046 3048 4001 4003 4007 4010 4012 4017 4024 4026 4027 4030 4032 4034 4037 4039 4044 6001 6003 6005 6008 6010 6013 6017 6023 6026 6031 6034 6040 6041 6044 6046 6048 7001 7002 7003 7007 7008 7010 7014 7016 7017 7018 7020 7021 7025 7027 7028 7030 7031 7033 7034 7036 7041 7042 7044 7048 7050

## Dimensions

Covariance Parameters	10
Columns in X	9
Columns in Z	0
Subjects	82
Max Obs Per Subject	2
Observations Used	164
Observations Not Used	0
Total Observations	164

Appendix 3

19:53 Monday, December 11, 2006 1368

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies  
 T0 = Baseline (A Covariate)

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	203.76835022	
1	2	135.23576994	0.00526554
2	1	134.74717989	0.00094759
3	1	134.66531068	0.00004513
4	1	134.66172084	0.00000013
5	1	134.66171114	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
Variance	PATIENT(STUDY)	STUDY 2	0.004515
CS	PATIENT(STUDY)	STUDY 2	-0.00123
Variance	PATIENT(STUDY)	STUDY 3	0.2346
CS	PATIENT(STUDY)	STUDY 3	0.02188
Variance	PATIENT(STUDY)	STUDY 4	0.2345
CS	PATIENT(STUDY)	STUDY 4	-0.06446
Variance	PATIENT(STUDY)	STUDY 6	0.1997
CS	PATIENT(STUDY)	STUDY 6	0.06526
Variance	PATIENT(STUDY)	STUDY 7	0.09736
CS	PATIENT(STUDY)	STUDY 7	0.04181

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

TO = Baseline (A Covariate)

## The Mixed Procedure

## Fit Statistics

-2 Res Log Likelihood	134.7
AIC (smaller is better)	154.7
AICC (smaller is better)	156.2
BIC (smaller is better)	178.7

## Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
9	69.11	<.0001

## Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
TO	1	76.9	6.55	0.0125
STUDY	4	35.3	4.02	0.0086
TREAT	1	13.6	0.66	0.4316

## Least Squares Means

Effect	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	-0.2226	0.03562	63	-6.25	<.0001	0.05	-0.2938	-0.1514
TREAT	Placebo	-0.1994	0.03567	63.4	-5.59	<.0001	0.05	-0.2707	-0.1282

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

## The Mixed Procedure

## Differences of Least Squares Means

Effect	TREAT	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	Placebo	-0.02317	0.02859	13.6	-0.81	0.4316	0.05	-0.08467	0.03832

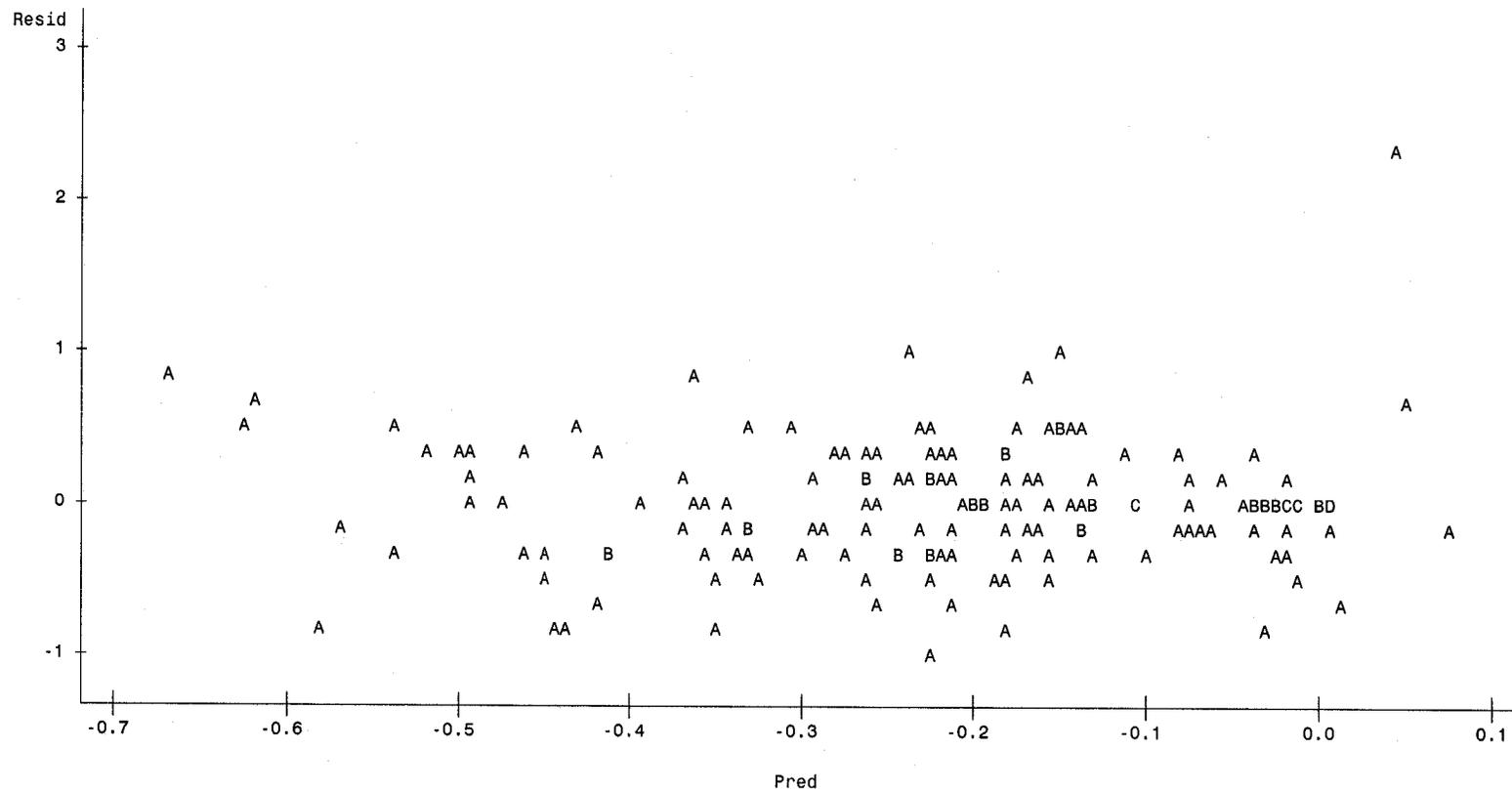
Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies  
T0 = Baseline (A Covariate)

Plot of Resid\*Pred. Legend: A = 1 obs, B = 2 obs, etc.



Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

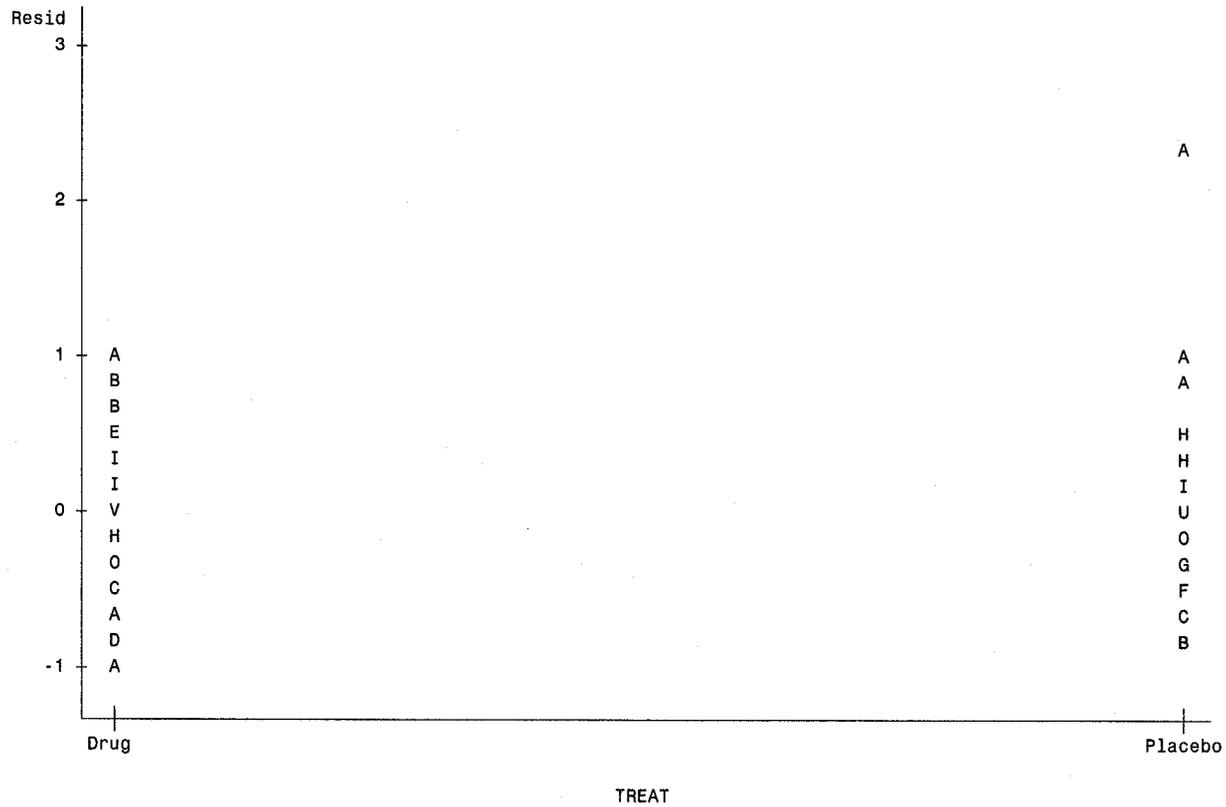
Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

Plot of Resid\*TREAT. Legend: A = 1 obs, B = 2 obs, etc.



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	-0.0092861	Sum Observations	-0.7614582
Std Deviation	0.39455935	Variance	0.15567708
Skewness	0.03128514	Kurtosis	0.26247897
Uncorrected SS	12.6169145	Corrected SS	12.6098435
Coeff Variation	-4248.9351	Std Error Mean	0.04357179

## Basic Statistical Measures

Location		Variability	
Mean	-0.00929	Std Deviation	0.39456
Median	-0.00150	Variance	0.15568
Mode	.	Range	1.92058
		Interquartile Range	0.48894

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----	
Student's t	t -0.21312	Pr >  t	0.8318
Sign	M 0	Pr >=  M	1.0000
Signed Rank	S -41.5	Pr >=  S	0.8492

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

## The UNIVARIATE Procedure

Variable: Resid

## Tests for Normality

Test	--Statistic--	-----p Value-----
Shapiro-Wilk	W 0.983726	Pr < W 0.3869
Kolmogorov-Smirnov	D 0.081033	Pr > D >0.1500
Cramer-von Mises	W-Sq 0.0934	Pr > W-Sq 0.1386
Anderson-Darling	A-Sq 0.519741	Pr > A-Sq 0.1899

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	1.00322173
99%	1.00322173
95%	0.60979268
90%	0.55894621
75% Q3	0.20437408
50% Median	-0.00149725
25% Q1	-0.28456865
10%	-0.43091800
5%	-0.75958162
1%	-0.91736042
0% Min	-0.91736042

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

## Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.917360	3015	72	0.609793	4017	6
-0.884814	3005	69	0.658367	6005	18
-0.874510	3001	67	0.802206	7042	63
-0.761838	4010	4	0.886518	3026	75
-0.759582	3008	70	1.003222	7018	51



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	0.00928608	Sum Observations	0.76145825
Std Deviation	0.43167492	Variance	0.18634324
Skewness	1.80749316	Kurtosis	8.58494679
Uncorrected SS	15.1008731	Corrected SS	15.0938022
Coeff Variation	4648.62565	Std Error Mean	0.04767052

## Basic Statistical Measures

Location		Variability	
Mean	0.00929	Std Deviation	0.43167
Median	-0.01308	Variance	0.18634
Mode	.	Range	3.09377
		Interquartile Range	0.42316

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----	
Student's t	t 0.194797	Pr >  t	0.8460
Sign	M -2	Pr >=  M	0.7407
Signed Rank	S -70.5	Pr >=  S	0.7467

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
 Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure  
 Variable: Resid

## Tests for Normality

Test		--Statistic--		-----p Value-----
Shapiro-Wilk	W	0.880967	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.116594	Pr > D	<0.0100
Cramer-von Mises	W-Sq	0.209523	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	1.336554	Pr > A-Sq	<0.0050

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	2.2804167
99%	2.2804167
95%	0.5766560
90%	0.4586484
75% Q3	0.2093479
50% Median	-0.0130752
25% Q1	-0.2138126
10%	-0.4487924
5%	-0.5950915
1%	-0.8133560
0% Min	-0.8133560

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure  
Variable: Resid

## Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.813356	6041	28	0.576656	4001	1
-0.802972	4017	6	0.577921	3036	77
-0.727444	7021	53	0.789166	4037	13
-0.601854	4003	2	1.032776	3023	74
-0.595092	6005	18	2.280417	6026	24

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction  
Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies  
T0 = Baseline (A Covariate)

TREAT=Placebo

The UNIVARIATE Procedure  
Variable: Resid

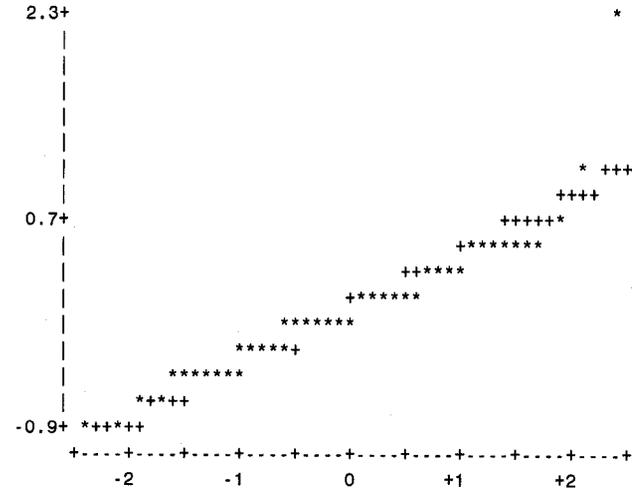
Stem Leaf	#
22 8	1
20	
18	
16	
14	
12	
10 3	1
8	
6 9	1
4 156679488	9
2 0145666895	10
0 1222345555233358	17
-0 887776420997754322210	21
-2 74005311	8
-4 055532220	9
-6 300	3
-8 10	2

-----+-----+-----+-----+  
Multiply Stem.Leaf by 10\*\*-1

Boxplot



Normal Probability Plot



Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

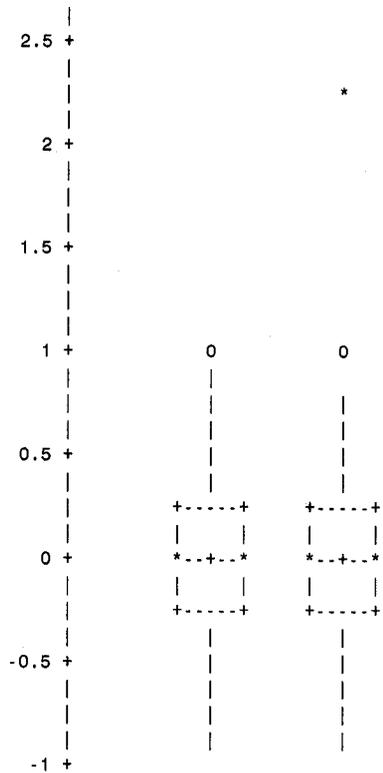
Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies

T0 = Baseline (A Covariate)

The UNIVARIATE Procedure

Variable: Resid

Schematic Plots



Appendix 3

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes  
Model 2: Fixed Effects Model, Adjusting for Baseline Nasal Airflow Resistance and Study without Treatment by Study Interaction

Patient Is Random

Assuming Within Subject Variance Component and Between Subject Variance Component Differ Across Studies  
TO = Baseline (A Covariate)

The UNIVARIATE Procedure

Variable: Resid

Schematic Plots

-----+-----+-----  
TREAT                    Drug                    Placebo

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

## The Mixed Procedure

## Model Information

Data Set	WORK.TEN_MG
Dependent Variable	LN240CHG
Covariance Structures	Variance Components, Compound Symmetry
Subject Effect	PATIENT(STUDY)
Group Effect	STUDY
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Prasad-Rao-Jeske- Kacker-Harville
Degrees of Freedom Method	Kenward-Roger

## Class Level Information

Class	Levels	Values
STUDY	5	2 3 4 6 7
TREAT	2	Drug Placebo

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

The Mixed Procedure

Class Level Information

Class	Levels	Values
PATIENT	82	2001 2005 2007 2012 2014 2018
		2020 2021 2023 2024 3001 3003
		3005 3008 3009 3015 3018 3023
		3026 3032 3036 3039 3041 3044
		3046 3048 4001 4003 4007 4010
		4012 4017 4024 4026 4027 4030
		4032 4034 4037 4039 4044 6001
		6003 6005 6008 6010 6013 6017
		6023 6026 6031 6034 6040 6041
		6044 6046 6048 7001 7002 7003
		7007 7008 7010 7014 7016 7017
		7018 7020 7021 7025 7027 7028
		7030 7031 7033 7034 7036 7041
		7042 7044 7048 7050

Dimensions

Covariance Parameters	12
Columns in X	4
Columns in Z	15
Subjects	1
Max Obs Per Subject	164
Observations Used	164
Observations Not Used	0
Total Observations	164

Appendix 3

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

The Mixed Procedure

Parameter Search

CovP1	CovP2	CovP3	CovP4	CovP5	CovP6	CovP7	CovP8	CovP9	CovP10	CovP11	CovP12	Res Log Like
0.2000	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000	0.2000	-123.7986

Parameter Search

-2 Res Log Like

247.5972

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
1	2	222.90819774	297.70460166
2	1	212.58046402	545.10633263
3	1	205.91697039	1234.8778267
4	1	200.91422586	2456.8934686
5	1	197.83523543	1616.8165934
6	1	191.02990173	16821.572073
7	1	187.63396623	1696.0509761
8	1	181.00219907	476.57577686
9	1	172.41670391	2358.0129409
10	1	168.94876423	4823.4423004
11	1	165.04552998	10903.190467
12	1	159.72675865	29702.355266
13	1	159.33456409	31034.792708
14	1	157.05933495	11758.801313
15	1	152.54662864	23582.458713

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

The Mixed Procedure

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
16	1	143.87531074	4320.4679411
17	3	139.13977683	2687.9821946
18	2	136.55116237	2148.3372023
19	2	134.41920976	1162.1559555
20	2	133.36775340	0.02597984
21	2	132.07866091	0.00751616
22	1	131.37260849	0.00059547
23	1	131.32027677	0.00000867
24	1	131.31955293	0.00000001

Convergence criteria met.

Estimated R Matrix  
for Subject 1

Row	Col1	Col2
1	0.003321	-0.00123
2	-0.00123	0.003321

Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
STUDY			0.01215
STUDY*TREAT			3.28E-18
Variance	PATIENT(STUDY)	STUDY 2	0.004554

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

## The Mixed Procedure

## Covariance Parameter Estimates

Cov Parm	Subject	Group	Estimate
CS	PATIENT(STUDY)	STUDY 2	-0.00123
Variance	PATIENT(STUDY)	STUDY 3	0.2301
CS	PATIENT(STUDY)	STUDY 3	0.01912
Variance	PATIENT(STUDY)	STUDY 4	0.2340
CS	PATIENT(STUDY)	STUDY 4	-0.06158
Variance	PATIENT(STUDY)	STUDY 6	0.1934
CS	PATIENT(STUDY)	STUDY 6	0.06922
Variance	PATIENT(STUDY)	STUDY 7	0.09593
CS	PATIENT(STUDY)	STUDY 7	0.04515

## Fit Statistics

-2 Res Log Likelihood	131.3
AIC (smaller is better)	153.3
AICC (smaller is better)	155.1
BIC (smaller is better)	149.0

## PARMS Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
11	116.28	<.0001

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

## The Mixed Procedure

## Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
TO	1	79.1	8.55	0.0045
TREAT	1	13.7	0.64	0.4361

## Least Squares Means

Effect	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	-0.2246	0.06124	4.13	-3.67	0.0203	0.05	-0.3926	-0.05662
TREAT	Placebo	-0.2016	0.06126	4.14	-3.29	0.0287	0.05	-0.3695	-0.03375

## Differences of Least Squares Means

Effect	TREAT	TREAT	Estimate	Standard Error	DF	t Value	Pr >  t	Alpha	Lower	Upper
TREAT	Drug	Placebo	-0.02300	0.02867	13.7	-0.80	0.4361	0.05	-0.08462	0.03862

Meta-Analysis of Phenylephrine vs. Placebo

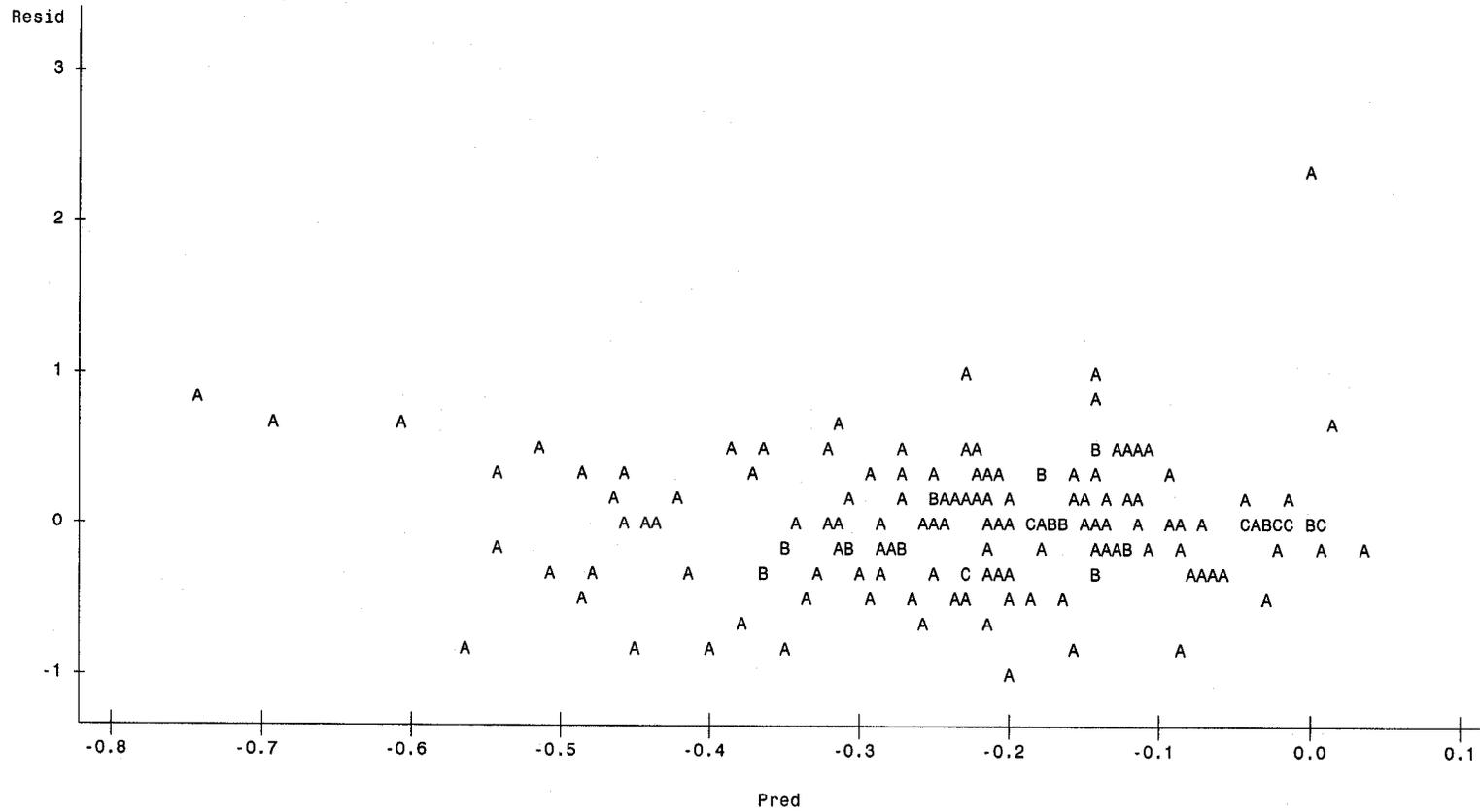
Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

Plot of Resid\*Pred. Legend: A = 1 obs, B = 2 obs, etc.



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Meta-Analysis of Phenylephrine vs. Placebo

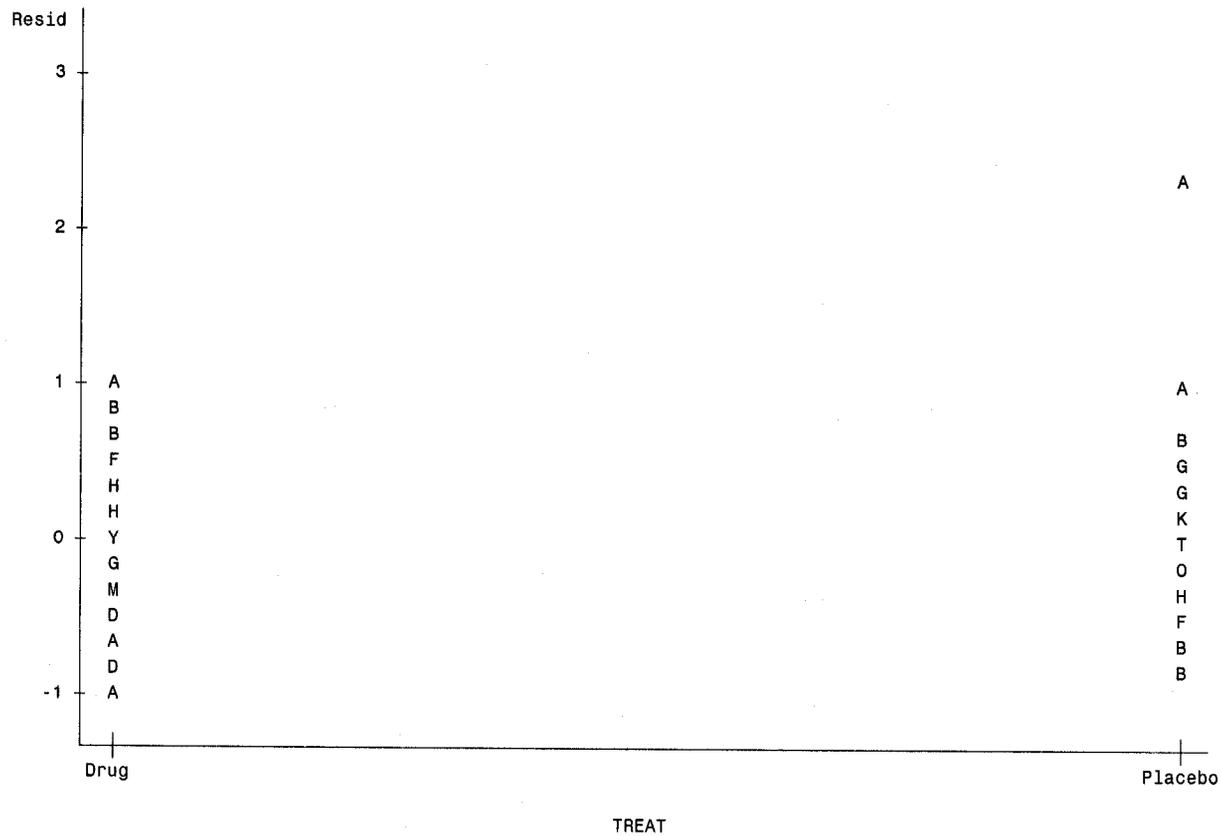
Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

T0 = Baseline (A Covariate)

Plot of Resid\*TREAT. Legend: A = 1 obs, B = 2 obs, etc.



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Drug -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	-0.0079704	Sum Observations	-0.6535719
Std Deviation	0.39719531	Variance	0.15776411
Skewness	-0.0134559	Kurtosis	0.26562363
Uncorrected SS	12.7841024	Corrected SS	12.7788932
Coeff Variation	-4983.3871	Std Error Mean	0.04386288

## Basic Statistical Measures

Location		Variability	
Mean	-0.00797	Std Deviation	0.39720
Median	0.00201	Variance	0.15776
Mode	.	Range	1.92880
		Interquartile Range	0.47283

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----
Student's t	t -0.18171	Pr >  t  0.8563
Sign	M 1	Pr >=  M  0.9122
Signed Rank	S -16.5	Pr >=  S  0.9398

Appendix 3

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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

Tests for Normality

Test		--Statistic--		-----p Value-----
Shapiro-Wilk	W	0.981634	Pr < W	0.2902
Kolmogorov-Smirnov	D	0.08883	Pr > D	0.1081
Cramer-von Mises	W-Sq	0.121284	Pr > W-Sq	0.0590
Anderson-Darling	A-Sq	0.619883	Pr > A-Sq	0.1037

Quantiles (Definition 5)

Quantile	Estimate
100% Max	0.99059542
99%	0.99059542
95%	0.59357977
90%	0.52633323
75% Q3	0.20452646
50% Median	0.00201472
25% Q1	-0.26830475
10%	-0.41881859
5%	-0.78668805
1%	-0.93820791
0% Min	-0.93820791

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

T0 = Baseline (A Covariate)

----- TREAT=Drug -----

The UNIVARIATE Procedure

Variable: Resid

Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.938208	3015	72	0.593580	4017	6
-0.885189	3005	69	0.695692	6005	18
-0.862107	3001	67	0.857325	3026	75
-0.805825	4010	4	0.870555	7042	63
-0.786688	3008	70	0.990595	7018	51

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Drug -----

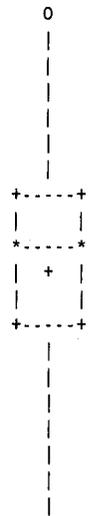
The UNIVARIATE Procedure

Variable: Resid

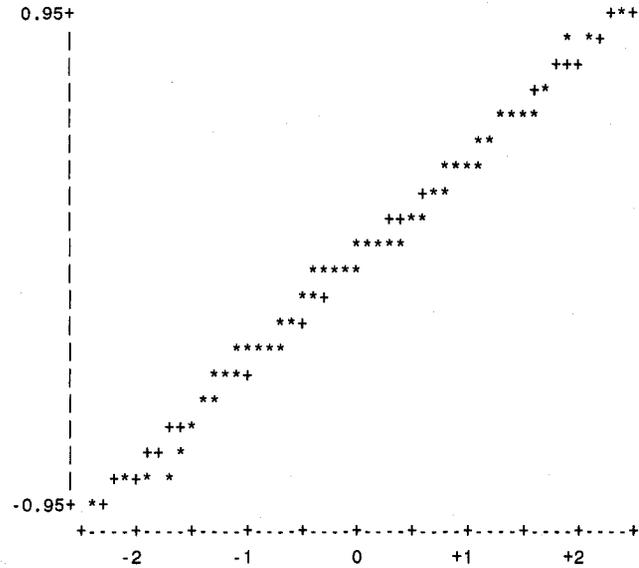
Stem Leaf	#
9 9	1
8 67	2
7 0	1
6	
5 33489	5
4 089	3
3 22378	5
2 0589	4
1 344669	6
0 000113334455778	15
-0 995433222110	12
-1 7531	4
-2 7665	4
-3 77753221	8
-4 2210	4
-5 51	2
-6 4	1
-7 9	1
-8 961	3
-9 4	1

-----+-----+-----+-----+  
 Multiply Stem.Leaf by 10\*\*-1

Boxplot



Normal Probability Plot



## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Moments

N	82	Sum Weights	82
Mean	0.01054269	Sum Observations	0.86450073
Std Deviation	0.43133125	Variance	0.18604665
Skewness	1.89016917	Kurtosis	9.2963805
Uncorrected SS	15.0788929	Corrected SS	15.0697787
Coeff Variation	4091.28199	Std Error Mean	0.04763257

## Basic Statistical Measures

Location		Variability	
Mean	0.01054	Std Deviation	0.43133
Median	-0.02020	Variance	0.18605
Mode	.	Range	3.14384
		Interquartile Range	0.40426

## Tests for Location: Mu0=0

Test	-Statistic-	-----p Value-----
Student's t	t 0.221334	Pr >  t  0.8254
Sign	M -2	Pr >=  M  0.7407
Signed Rank	S -69.5	Pr >=  S  0.7501

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

T0 = Baseline (A Covariate)

----- TREAT=Placebo -----

## The UNIVARIATE Procedure

Variable: Resid

## Tests for Normality

Test		--Statistic---		-----p Value-----
Shapiro-Wilk	W	0.875939	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.101707	Pr > D	0.0356
Cramer-von Mises	W-Sq	0.19516	Pr > W-Sq	0.0060
Anderson-Darling	A-Sq	1.29256	Pr > A-Sq	<0.0050

## Quantiles (Definition 5)

Quantile	Estimate
100% Max	2.3227348
99%	2.3227348
95%	0.5513534
90%	0.4397340
75% Q3	0.1983180
50% Median	-0.0202032
25% Q1	-0.2059465
10%	-0.4740199
5%	-0.5486008
1%	-0.8211029
0% Min	-0.8211029

## Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure

Variable: Resid

## Extreme Observations

-----Lowest-----			-----Highest-----		
Value	PATIENT	Obs	Value	PATIENT	Obs
-0.821103	4017	6	0.551353	4001	1
-0.759694	6041	28	0.608060	7042	63
-0.726732	7021	53	0.736742	4037	13
-0.645542	4003	2	1.018486	3023	74
-0.548601	6005	18	2.322735	6026	24

Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

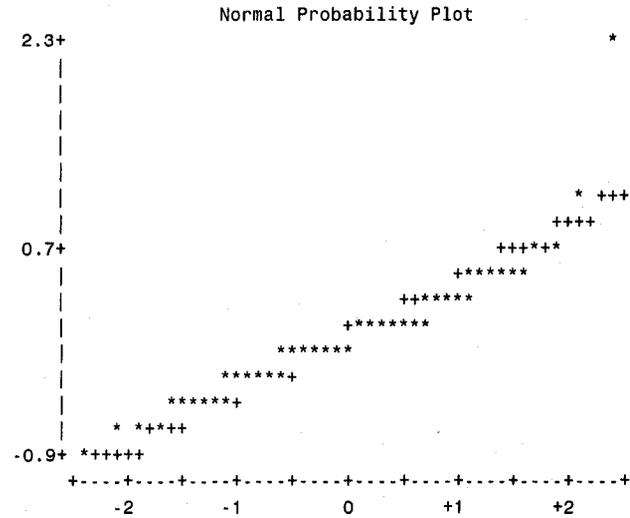
TO = Baseline (A Covariate)

----- TREAT=Placebo -----

The UNIVARIATE Procedure  
Variable: Resid

Stem Leaf	#	Boxplot
22 2	1	*
20		
18		
16		
14		
12		
10 2	1	0
8		
6 14	2	
4 3346955	7	
2 0455560346	10	+-----+
0 112224455613357899	18	+
-0 77654321098664432221	20	*-----*
-2 985543051110	12	+-----+
-4 5108720	7	
-6 635	3	
-8 2	1	0

-----+-----+-----+-----+  
Multiply Stem.Leaf by 10\*\*-1



Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

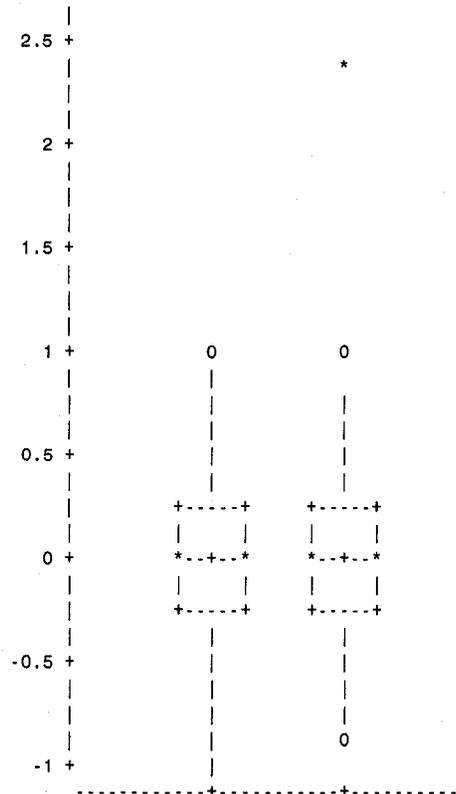
Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

The UNIVARIATE Procedure

Variable: Resid

Schematic Plots



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Meta-Analysis of Phenylephrine vs. Placebo

Performing Analysis of Covariance by Time Point: LN-Ratio (Post-baseline Nasal Airflow Resistance / Baseline Nasal Airflow Resistance) at 240 Minutes

Model 3: Random Effects Model, Adjusting for Baseline Nasal Airflow Resistance

Patient, Study, and Study by Treatment Interaction Are Random

TO = Baseline (A Covariate)

The UNIVARIATE Procedure

Variable: Resid

Schematic Plots

TREAT                      Drug      Placebo