



An Efficient Way for Statistical Review Using the RShiny Application

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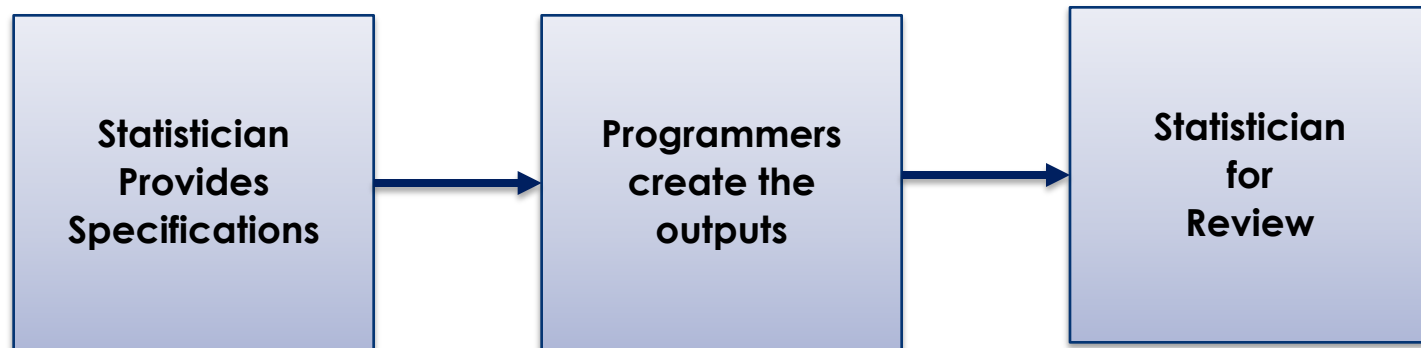
Agenda

- Usual Process of Review
- Idea of the application
- Why R-Shiny?
- Overview of the application
- Process flow using application
- Illustrations
- Conclusion

Introduction

In this presentation we will discuss about an application created using R Shiny, which will help statistician review the outputs efficiently.

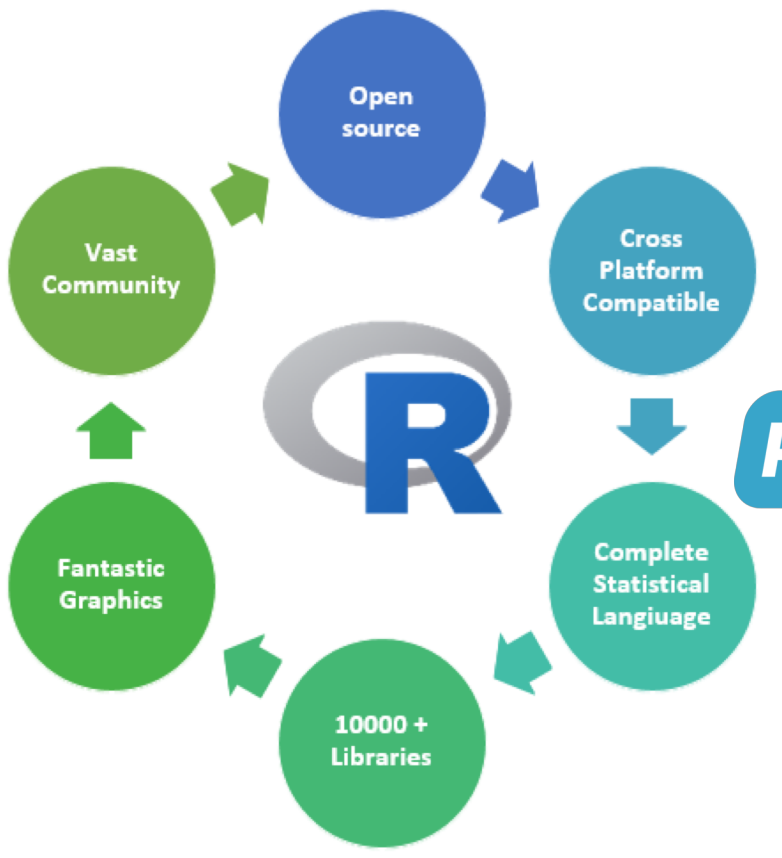
Usual Process of Review



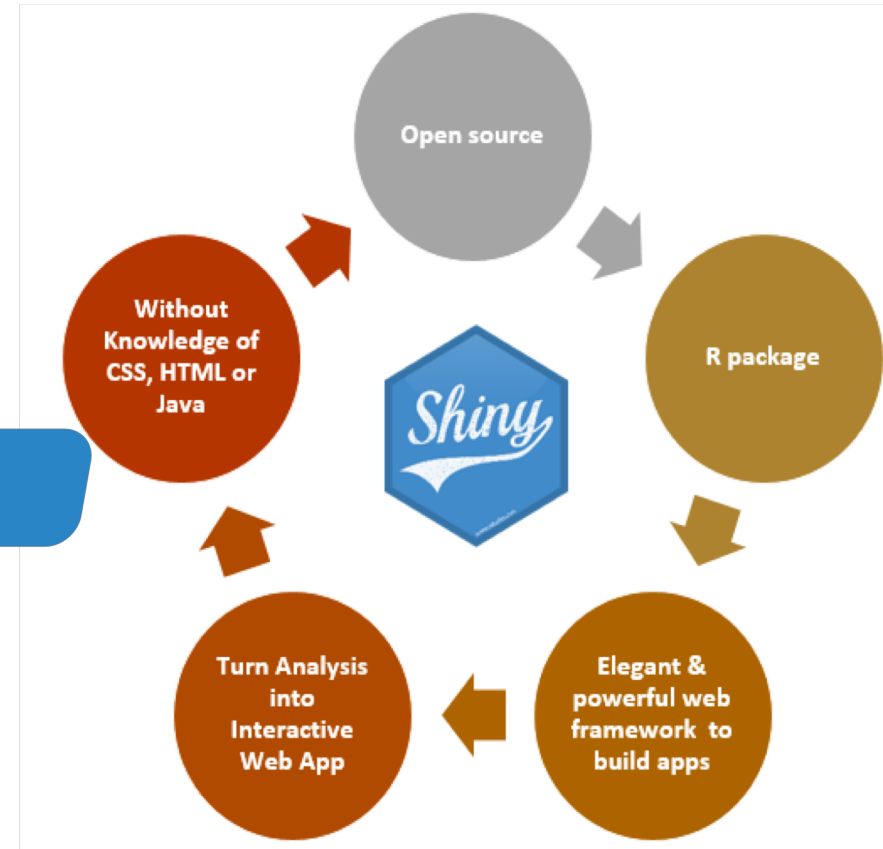
Idea of the application

- Usually Statisticians review critical reports
 - Includes results from Statistical tests or model based analysis
 - Independent programming to review the results – ensure accuracy
- Time saving
- Very much helpful in case of tight timelines
- Can we get the results quickly or just with the click

Why R-Shiny?



PLUS



Overview of the application

- Focuses on various statistical tests used for efficacy checking and treatment comparisons
- Model-based analysis
- It can perform range of statistical tests like-
 - One Sample t-test
 - Two Sample t-test
 - Paired t-test
 - Wilcoxon Signed Rank test
 - Mann-Whitney (Wilcoxon Rank Sum) test
 - Friedman test
 - PK parameter comparison
 - Dose Proportionality

Process flow using application

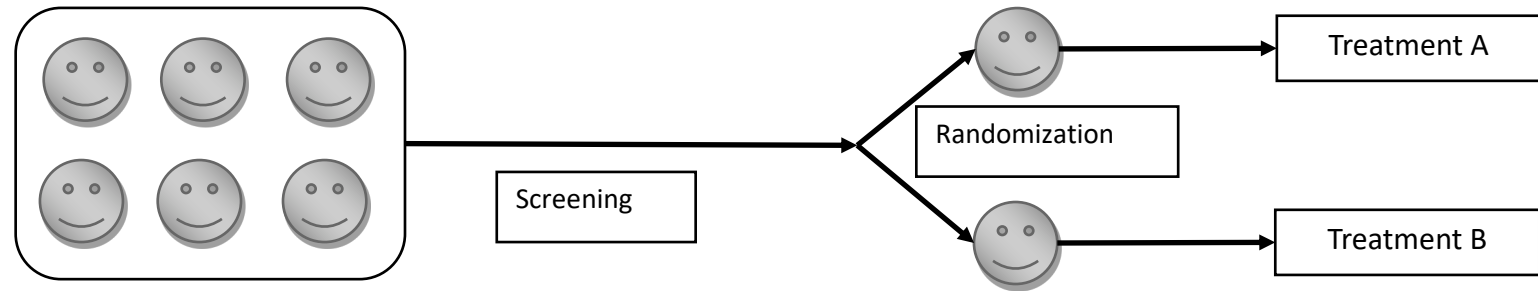
- Dataset- SAS, Excel or CSV
- Import the appropriate data
- Select the desired statistical test
- Specify the key requirements-
 - Response variable
 - Class variable
 - By variables
 - Random effect (in case of model analysis)
 - Significance level (alpha)
 - If model-based analysis then write the model
- Click Submit – Results get displayed in the application

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- Results can be cross-checked
- Download results as csv file
- We have deployed use of this application for different statistical tests

Illustration 1 - Simple Parametric tests

Study design-



- Objective was to compare two treatments A & B
- The endpoint of interest was Skin Appearance measured on continuous scale by a particular device
- As per SAP, '*Two Sample t-test for unpaired data*' was used
- The hypothesis of interest was – Two treatments show different effects.

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Results from Report

Treatment Comparison- Two-Sample t-test Skin Appearance: CFB Values						
Comparison	Timepoint	Mean Difference	t-Value	95% LCL	95% UCL	p-Value (Two Sided)
Treatment A Vs. Treatment B	15 Minutes Post Product application	-0.15	-1.01	-0.45	0.15	0.3150
	Day 4	-0.18	-0.18	-0.14	0.11	0.8553
	Week 1	-0.083	-1.28	-0.21	0.046	0.2048
	Week 4	-0.056	-1.14	-0.15	0.042	0.2575
	Week 8	-0.059	-0.73	-0.22	0.10	0.4675
	Week 12	-0.36	-3.05	-0.59	-0.12	0.0030

SE = Standard Error, LCL = Lower Confidence Limit, UCL = Upper Confidence Limit

Results from Application

endpoint	timenum	timepoint	Product_pair	Mean	tValue	Probt	alpha	lower	upper
1 Skin Appearance	2	15 Minutes Post Product Application	Treatment A - Treatment B	-0.15032980	-1.0107607	0.315011498	0.05	-0.4460613	0.14540174
2 Skin Appearance	3	Day 4	Treatment A - Treatment B	-0.01137592	-0.1828323	0.855391332	0.05	-0.1351954	0.11244357
3 Skin Appearance	4	Week 1	Treatment A - Treatment B	-0.08298167	-1.2766700	0.204799610	0.05	-0.2120034	0.04604004
5 Skin Appearance	5	Week 4	Treatment A - Treatment B	-0.05632175	-1.1395597	0.257496817	0.05	-0.1545128	0.04186933
6 Skin Appearance	6	Week 8	Treatment A - Treatment B	-0.05923936	-0.7303770	0.467523177	0.05	-0.2209174	0.10243871
4 Skin Appearance	7	Week 12	Treatment A - Treatment B	-0.35908742	-3.0456152	0.003039947	0.05	-0.5932979	-0.12487689

Continued...

Two Sample T-Test

The TTEST Procedure

Variable: CFB

Endpoint=Skin Appearance Timenum=2 Timepoint=15 Minutes Post Product Application

Treatment	N	Mean	Std Dev	Std Err	Minimum	Maximum
Treatment A	50	1.1332	0.5895	0.0834	0.1130	3.1270
Treatment B	49	1.2835	0.8622	0.1232	0.1630	4.0270
Diff (1-2)		-0.1503	0.7371	0.1482		

Treatment	Method	Mean	95% CL Mean	Std Dev	95% CL Std Dev
Treatment A		1.1332	0.9656 1.3007	0.5895	0.4924 0.7346
Treatment B		1.2835	1.0358 1.5311	0.8622	0.7190 1.0771
Diff (1-2)	Pooled	-0.1503	-0.4444 0.1438	0.7371	0.6464 0.8577
Diff (1-2)	Satterthwaite	-0.1503	-0.4461 0.1454		

Method	Variances	DF	t Value	Pr > t
Pooled	Equal	97	-1.01	0.3129
Satterthwaite	Unequal	84.649	-1.01	0.3150

Equality of Variances				
Method	Num DF	Den DF	F Value	Pr > F
Folded F	48	49	2.14	0.0091

Illustration 2- Non-parametric test

- The endpoint of interest was Skin Appearance Grade given by Dermatologist on ordinal scale
- As per SAP, 'Mann-Whitney (Wilcoxon Rank Sum) test' was used

Treatment Comparison - Wilcoxon Rank Sum Test (Mann-Whitney Test)										
Skin Appearance Grade: CFB Values										
		N		Mean		Sum of Scores				
Comparison	Timepoint	Treatment A	Treatment B	Treatment A	Treatment B	Treatment A	Treatment B	Mean Difference (Treatment A – Treatment B)	Z-Stat	p-Value (Two Sided)
Treatment A Vs. Treatment B	15 Minutes Post Product application	49	49	-0.59	-0.58	2422.50	2428.50	-0.01	-0.02	0.9836
	Day 4	49	49	-0.07	-0.21	2708.00	2143.00	0.14	2.36	0.0183
	Week 1	48	49	-0.09	-0.17	2555.00	2198.00	0.07	1.28	0.1996
	Week 4	47	48	-0.20	-0.26	2365.00	2195.00	0.06	0.49	0.6253
	Week 8	47	47	-0.18	-0.39	2499.00	1966.00	0.21	2.13	0.0330
	Week 12	46	47	-0.12	-0.43	2554.50	1816.50	0.32	2.81	0.0050

Z-stat and p-values are based on Wilcoxon Rank Sum test and not on Mean.
N= Number of Subjects.

endpoint	Timenum	timepoint	n1	n2	mean1	mean2	mean_diff	sum.rank.a1	sum.rank.b1	Z	p_value
1 Skin Appearance Grade	1	15 Minutes Post Product Application	49	49	-0.59183674	-0.5816327	-0.01020408	2422.5	2428.5	-0.02050425	0.983641126
2 Skin Appearance Grade	2	Day 4	49	49	-0.07142857	-0.2142857	0.14285714	2708.0	2143.0	2.36003369	0.018273276
3 Skin Appearance Grade	3	Week 1	49	48	-0.09183674	-0.1666667	0.07482993	2555.0	2198.0	1.28261613	0.199626595
4 Skin Appearance Grade	4	Week 4	48	47	-0.19791667	-0.2553191	0.05740248	2365.0	2195.0	0.48833401	0.625313277
5 Skin Appearance Grade	5	Week 8	47	47	-0.18085106	-0.3936170	0.21276596	2499.0	1966.0	2.13230804	0.032981532
6 Skin Appearance Grade	6	Week 12	47	46	-0.11702128	-0.4347826	0.31776133	2554.5	1816.5	2.80658282	0.005007004

Illustration 3- Model-based analysis

- Let us see one model-based analysis results
- As per SAP model to be used was, natural log transformed PK parameter values as response variable, treatment as fixed effect, baseline as covariate and subject as random effect at confidence level of 90%

Summary of Pharmacokinetic Parameters

Pharmacokinetic Parameter	Treatment					
	Treatment A			Treatment B		
	N	GM	90% CI	N	GM	90% CI
AUC _{inf} [†] (hr.ng/mL)	24	20.70	(19.07, 22.46)	24	24.82	(23.17, 26.59)
AUC _{last} [†] (ng/mL)	23	20.41	(18.81, 22.14)	21	24.49	(22.83, 26.26)
C _{max} [†] (ng/mL)	24	2.75	(2.50, 3.03)	23	3.36	(3.13, 3.60)
[†] Back-transformed least squares mean and confidence interval from ANCOVA model performed on natural log-transformed values. GM: Geometric Mean CI: Confidence Interval						

	Param	gm_trta	lower_trta	upper_trta	gm_trtb	lower_trtb	upper_trtb
1	AUCInf	20.697841	19.072186	22.46206	24.825366	23.172783	26.595804
2	AUCLast	20.409305	18.809151	22.14559	24.488681	22.836083	26.260873
3	Cmax	2.749592	2.495637	3.02939	3.355265	3.129544	3.597266

Conclusion

- This application is useful to review outputs
- Covers basic statistical tests and complex model-based analysis too
- Saves lot of time and efforts – results are just a click away
- Can be used to catch potential programming errors
- Strengthens the review process as totally different software is used to verify the results

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3. Application Development Framework for R/Shiny- PharmaSUG
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Thank You

Any Questions?

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