

PPII: Comparison of different SAS procedures for conducting statistical hypothesis tests and calculation of 95% confidence intervals in clinical trials



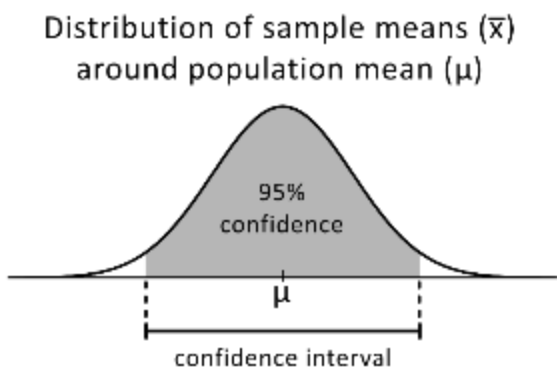
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Introduction

Statistical hypothesis tests are an important part of clinical research and they are commonly used by investigators in reporting the results of clinical trials. Along with standard data step functions allowing to conduct statistical hypothesis tests, there are stand alone statistical procedures provided by SAS that are intended to do the same but with a much greater flexibility and convenience.

There are a variety of confidence intervals, so the analyst must determine which type of interval to use depending on the application. Two commonly used types are confidence intervals for population parameters and confidence intervals for distribution percentiles. The most frequently used type of confidence interval attempts to capture the population mean.

All statistical intervals have an associated confidence level. The analyst must determine the confidence level based on what seems to be an acceptable degree of assurance for the specific application. For instance, the analyst may construct a 95% confidence interval for the mean. This indicates that the method of construction guarantees that 95% of all such intervals will contain the (true) population mean.

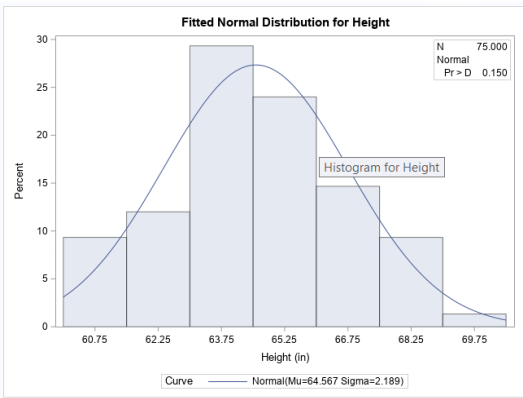


Proc univariate is more flexible and gives more options for the analysis, for example it provides test for normality

```
proc univariate data=Heights cibasic;  
var Height;  
run;  
  
proc univariate data=Heights cibasic(alpha=.02);  
var Height;  
run;  
  
proc univariate data=Heights;  
  histogram Height /  
  normal(percent=20 40 60 80 midpercent)  
  odstitle = title;  
  inset n normal(ksdpval) /  
  pos = ne format = 6.3;  
run;
```

Basic Confidence Limits Assuming Normality			
Parameter	Estimate	95% Confidence Limits	
Mean	64.56667	64.06302	65.07031
Std Deviation	2.18900	1.88608	2.60874
Variance	4.79171	3.55731	6.80552

Basic Confidence Limits Assuming Normality			
Parameter	Estimate	98% Confidence Limits	
Mean	64.56667	63.96564	65.16769
Std Deviation	2.18900	1.83590	2.69929
Variance	4.79171	3.37053	7.28617



Proc univariate also provides distribution-free confidence intervals for standard percentiles (quartiles) and can compute confidence intervals for a specified list of percentiles.

```
proc univariate plot data = alb cipctldf;  
var aval ;  
run ;
```

Quantiles (Definition 5)					
Level	Quantile	95% Confidence Limits		Order Statistics	
		Distribution Free		LCL Rank	UCL Rank
100% Max	3.5750				
99%	3.5720	3.564	3.575	98	100
95%	3.5530	3.536	3.575	91	100
90%	3.5355	3.528	3.561	85	97
75% Q3	3.5165	3.512	3.525	67	84
50% Median	3.4960	3.484	3.505	41	61
25% Q1	3.4695	3.461	3.478	17	34
10%	3.4575	3.441	3.461	4	16
5%	3.4430	3.428	3.457	1	10
1%	3.4295	3.428	3.439	1	3
0% Min	3.4280				

Proc ttest performs t tests for one sample, two samples, and paired observations. The one-sample t test compares the mean of the sample to a given number. The two-sample t test compares the mean of the first sample minus the mean of the second sample to a given number. The paired observations t test compares the mean of the differences in the observations to a given number.

```
data res;  
input AVAL1 AVAL2 @@;  
datalines;  
4.368 4.328 4.509 4.516 4.361 4.392 4.378 4.556 4.382 4.512  
4.390 4.367 4.398 4.519 4.503 4.369 4.397 4.395 4.518 4.524  
4.358 4.378 4.334 4.500 4.339 4.525 4.361 4.389 4.513 4.370  
4.561 4.506 4.333 4.379 4.523 4.541 4.501 4.395 4.334 4.358  
4.381 4.397 4.361 4.514 4.528 4.396 4.544 4.350 4.516 4.376  
4.512 4.550 4.331 4.531 4.569 4.541 4.368 4.563 4.522 4.520  
4.505 4.524 4.375 4.370 4.357 4.546 4.528 4.377 4.546 4.391  
4.510 4.361 4.341 4.502 4.391 4.506 4.349 4.514 4.396 4.549  
4.369 4.381 4.515 4.545 4.360 4.575 4.388 4.515 4.383 4.382  
4.517 4.384 4.367 4.367 4.502 4.371 4.516 4.373 4.500 4.366  
;  
run;  
  
proc ttest data = res ;  
var aval1*aval2 ;  
run ;
```

Difference: AVAL1 - AVAL2					
N	Mean	Std Dev	Std Err	Minimum	Maximum
50	-0.0150	0.1182	0.0167	-0.2150	0.1940
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.0150	-0.0485 0.0186	0.1182	0.0987	0.1473	
DF	t Value	Pr > t			
49	-0.90	0.3751			

Objective

To discuss and compare the capabilities and results of the procedures that are used to test statistical hypotheses and illustrate the calculation of confidence intervals by providing sample SAS code and output.

We can use **proc means** to get various summary statistics in a compact way, and 95% CI included.

```
data Heights;  
label Height = 'Height (in)';  
input Height @@;  
datalines;  
64.1 60.9 64.1 64.7 66.7 65.0 63.7 67.4 64.9 63.7  
64.0 67.5 62.8 63.9 65.9 62.3 64.1 60.6 68.6 68.6  
63.7 63.0 64.7 68.2 66.7 62.8 64.0 64.1 62.1 62.9  
62.7 60.9 61.6 64.6 65.7 66.6 66.7 66.0 68.5 64.4  
60.5 63.0 60.0 61.6 64.3 60.2 63.5 64.7 66.0 65.1  
63.6 62.0 63.6 65.8 66.0 65.4 63.5 66.3 66.2 67.5  
65.8 63.1 65.8 64.4 64.0 64.9 65.7 61.0 64.1 65.5  
68.6 66.6 65.7 65.1 70.0  
;  
run;
```

```
proc means data=Heights n mean clm ;  
var Height;  
run ;  
  
proc means data=Heights n mean clm alpha=0.02;  
var Height;  
run ;
```

The MEANS Procedure			
Analysis Variable : Height Height (in)			
N	Mean	Lower 95% CL for Mean	Upper 95% CL for Mean
75	64.5666667	64.0630240	65.0703093

The MEANS Procedure			
Analysis Variable : Height Height (in)			
N	Mean	Lower 98% CL for Mean	Upper 98% CL for Mean
75	64.5666667	63.9656446	65.1676887

CI can be used in one-sample t-tests. For example, during the research we have the assumption that patients with disease A have an average albumin level equals 3.5, and we want to test this hypothesis:

$$H_0: \mu = \mu_0$$
$$H_a: \mu \neq \mu_0$$

```
data ALB;  
input AVAL @@;  
label AVAL = 'Albumin (gm/dL)';  
datalines;  
3.468 3.428 3.509 3.516 3.461 3.492 3.478 3.556 3.482 3.512  
3.490 3.467 3.498 3.519 3.504 3.469 3.497 3.495 3.518 3.523  
3.458 3.478 3.443 3.500 3.449 3.525 3.461 3.489 3.514 3.470  
3.561 3.506 3.444 3.479 3.524 3.531 3.501 3.495 3.443 3.458  
3.481 3.497 3.461 3.513 3.528 3.496 3.533 3.450 3.516 3.476  
3.512 3.550 3.441 3.541 3.569 3.531 3.468 3.564 3.522 3.520  
3.505 3.523 3.475 3.470 3.457 3.536 3.528 3.477 3.536 3.491  
3.510 3.461 3.431 3.502 3.491 3.506 3.439 3.513 3.496 3.539  
3.469 3.481 3.515 3.535 3.460 3.575 3.488 3.515 3.484 3.482  
3.517 3.483 3.467 3.467 3.502 3.471 3.516 3.474 3.500 3.466  
;  
run;
```

```
Approach 1  
proc univariate data=alb mu0 = 3.5 ;  
var AVAL;  
run ;
```

Tests for Location: Mu0=3.5			
Test	Statistic	p Value	
Student's t	t -1.45406	Pr > t	0.1491
Sign	M -5	Pr >= M	0.3634
Signed Rank	S -437.5	Pr >= S	0.1216

```
Approach 2  
proc means data=alb n mean stddev clm alpha = .05 ;  
var AVAL ;  
run ;
```

The MEANS Procedure				
Analysis Variable : AVAL Albumin (gm/dL)				
N	Mean	Std Dev	Lower 95% CL for Mean	Upper 95% CL for Mean
100	3.4953300	0.0321169	3.4889573	3.5017027

Conclusion

Confidence intervals are generally more informative than p-values. They provide quantitative bounds that express the uncertainty inherent in estimation, instead of merely an accept or reject statement. Therefore, reporting of confidence intervals along with significance tests will improve the understanding of the findings from clinical trials.

There are multiple approaches in SAS to calculate confidence intervals: **PROC MEANS** is the most convenient method for generating compact, quick analysis without providing details and assuming that data is distributed normally; **PROC UNIVARIATE** is very flexible instrument that provides both distribution-dependent and distribution-free analysis, also can be used to test data for normality; **PROC TTEST** is the most practical to perform t-tests for one sample, two samples, and paired observations and can provide result for 95% CL.