SAMPLE SIZE DETERMINATION PROCEDURES IN CLINICAL TRIALS: A COMPARATIVE ANALYSIS FOR RELIABLE AND VALID RESEARCH RESULTS

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Abstract

Accurate sample size determination is paramount in clinical trials assuring the consistency and validity of research studies. This comparative analysis delves into the various procedures employed for sample size estimation in clinical trials and assesses their effectiveness in producing reliable results. By numerous formulaes and methods, this study seeks to identify best practices for optimizing sample sizes, thereby enhancing the statistical power of clinical trials. This research paper aims to conduct a comparative analysis of different formulae commonly employed in determining sample sizes evaluating their strengths, limitations, and applicability across various research scenarios. Several formulae have been considered with varying parameters, and the sample size was calculated and presented in different graphs.

Keywords: Sample Size, Population estimation, Sensitivity, Specificity, Experimental design

1. Introduction

Sample size refers to the volume of observations, units, or individuals included in a study,and the Sample size is a crucial step while doing experiments like Small-scale experiments, large-scale experiments, pilot studies, clinical trials, etc. A large sample size gives accurate and reliable outcomes and boosts statistical test precision. The test can detect an actual effect. We need to consider some important components in finding the exact sample size, including population size, variability of the data, desired level of precision, confidence level, research objectives, types of data, and analysis and resources available. Generally, a larger population indicates the least variability in the data. So, if the population is large, the sample should also be large to give the desired level of accuracy. The spread of the data points increases with the degree of data dispersion. To eradicate the problem of variability we have to use appropriate Statistical techniques. The level of precision specifies the closeness of the

sample estimate and population estimate. In this process, the discrepancy between the sample and the actual population is referred to as the sampling error. We can add or subtract 3% from the value in a survey if the sampling error is ±3%. For instance, 77% of students in a district get distinction marks in an exam, we can say, that between 74% and 80% of students get distinction marks. The reliability level tells us the probability that the target population parameters fall inside a scope of values. It is expressed in percentages like 90%, 95%, or 99%. The greater level of certainty in the results depends on a higher confidence level. Proper Research objectives should be defined clearly. The type of data and analysisare important aspects in the selection of a sample. The study also heavily weighs resources like personnel, money, and time. Therefore, it is crucial to use the resources at our disposal to achieve the appropriate degree of accuracy in our outcomes.

The sample size is considered an important factor when designing experiments or conducting clinical trials. Here few authors expressed their views in the nail down the difficulty of the preference of sampling size in the medical field. Halperin*et al.* [11] and Brown *et al.* [2] by utilizing the values of alpha and beta errors, found the size of a sample. Morse [21] described which factors need to be considered in the determination of sample size. Lenth [20] clearly described different aspects that lead to findinganappropriate sample size and he studied the power of a test of hypothesis to identifyaneffective sample size. Tatiana [34] explained the importance of the selection of samples and provided books to estimate study sizes like Fliess and Bland, and also provided software programs like EpiInfo and nQuery. Eng [8] elaborated on the essentiality of sample size, how to minimize sample size, and parameters that need to be considered and provided sample size formulas for comparative along with descriptive studies. Sakpal [31] calculated sample size by comparing two proportions and two means and gave basic rules for estimating sample size. Rohrig *et al.* [30] compared two drugsusing a t-test and explained the sample size principles,which require the power and rejection region of the statistical test. Ahmad *et al.* [1] suggested formulas for single and two ratios and took one instance from medical research to find an adequate sample size. Further, several authors have contributed towards the sample size determination size such as Lachenbruch [19], Obuchowski [26], Wittes [35], Whitley and Ball [36], Williamson [37], Pezeshk [27], Julius and Patterson [17], Chadha [5], Brutti *et al.* [3], Hertzog [12], Willan and Kowgier [38], Charles *et al.* [6]. Prajapati *et al.* [28], Mason, M. [22], Hajian-Tilaki [13], Burmeister and Aitken [4], Pourhoseingholi *et al.* [29], Hajian-Tilaki [15], Juneja and Sharma [18], Sami *et al.* [33], Negida *et al.* [23], Greene [10], Nanjundeswaraswamy and Divakar [25]. Hayat [14] and Singh and Masuku [32] clearly explained the significance of sample size and interpreted the key concepts involved in the establishment of sample size. Charan and Biswas [7] rationalized the effectiveness of sample size and provided information on different methods of sample size calculations for different studies and gave formulas accordingly. Negida [24] justified the sample size calculation in clinical studies by applying a software called StatsDirect to identify sample size using a correlation coefficient between two variables. We go through in detail of the following research papers.

In this paper, we have comprised several ways to estimate the sample size for any study. Glenn D. Israel [9] explained the criteria for concluding the sample size, which is affected by factors like thestudy's objective, population size, the problem of choosing an inappropriate sample, and Bias in sampling. He reviewed the accuracy, confidence, and variability levelsbriefly, which are very important points in judging the sample size. It also explains different proposals for resolving sample size issues.

2. Different approaches for estimation

The formula for computing a sample for ratios (Cochran1963:75)

$$n_0 = \frac{Z^2 pq}{e^2} \tag{1}$$

where,
n_0 = sample size
Z^2 = Normal curves abscissa
p = Estimated prevalence rate
q = 1- estimated prevalence rate

The Finite population correction for ratios is

$$n = \frac{n_0}{1+\frac{n_0 - 1}{N}} \tag{2}$$

Also, the Simplified formula for ratios (Yamane 1967:886):

$$n = \frac{N}{1+N(e)^2} \tag{3}$$

where,
n = sample number
N = Population count
e = Level of accuracy
Furthermore, the sample size formula for the mean is

$$n_0 = \frac{Z^2 \sigma^2}{e^2} \tag{4}$$

where,
σ^2 = variance of an attribute in the population
The following table 1 presents the sample size estimation at different values of related parameters namely sample proportions, the finite population correction, the streamlined formula for proportions, and samples for the mean, sample size estimate is performed for various values of the unknowns.

Table 1: *Sample size estimation at different values of related parameters*

p	0.99	0.93	0.88	0.85	0.77	0.73	0.69	0.63	0.61	0.59	0.56	0.46	0.54	0.49	0.5
q	0.01	0.07	0.12	0.15	0.23	0.27	0.31	0.37	0.39	0.41	0.44	0.54	0.46	0.51	0.5
N1	15	100	162	196	272	303	329	358	366	372	379	382	382	384	384
N2	14	83	134	164	224	252	277	304	315	324	333	339	349	357	361
N	250	500	750	1000	1250	1500	1750	2000	2250	2500	2750	3000	4000	5000	6000
N3	154	222	261	286	303	316	326	333	340	345	349	353	364	370	375
$\boldsymbol{\sigma^2}$	0.3	0.37	0.41	0.49	0.53	0.59	0.61	0.68	0.71	0.77	0.80	0.84	0.90	0.96	0.99
N4	138	210	258	369	432	535	572	711	775	911	983	1084	1245	1416	1506

Where,
N = Population count

p = estimated proportion of an attribute
$q = 1 - p$
N_1 = Sample for ratios
N_2 = finite population correction for ratios
N_3 = stream lined formula for proportions
N_4 = Sample for the mean

Baoliang Zhong [39] explained the sample size assessment in a Randomized controlled trial (RCT). The gold standard for establishing whether a treatment has a meaningful impact is to analyze the results of two groups using RCT. In RCT design, he explained four statistical conceptions, including H_0 and H_1, size of the critical region, and False negative. The Table 2 presents several formulae for dichotomous and continuous variable behaviour.

Table 2: *Basic General formulae for sample size calculation are as follows*

	Dichotomous variable	**Continuous variable**
Non – inferiority design*	$N = 2 \times \left[\frac{Z_{1-\alpha} + Z_{1-\beta}}{\gamma_0} \right]^2 \times t(1-t)$	$N = 2 \times \left[\frac{Z_{1-\alpha} + Z_{1-\beta}}{\gamma_0} \right]^2 \times s^2$
Equivalence design**	$N = 2 \times \left[\frac{Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}}{\gamma_0} \right]^2 \times t(1-t)$	$N = 2 \times \left[\frac{Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}}{\gamma_0} \right]^2 \times s^2$
Statistical superiority design***	$N = \frac{1}{2} \times \left[\frac{Z_{\frac{\alpha}{2}} + Z_{\beta}}{\arcsin\sqrt{t} - \arcsin\sqrt{t_0}} \right]^2$	$N = 2 \times \left[\frac{Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}}{\gamma} \right]^2 \times s^2$
Clinical superiority design****	$N = 2 \times \left[\frac{Z_{1-\alpha} + Z_{1-\beta}}{d - \gamma_0} \right]^2 \times t(1-t)$	$N = 2 \times \left[\frac{Z_{1-\alpha} + Z_{1-\beta}}{\gamma - \gamma_0} \right]^2 \times s^2$

Where,
N represents the size per group
t represents the response rate of the control group receiving the standard treatment
t_0 represents the response rate of the experiment group receiving the new drug treatment
d signifies the actual difference between the treatment effects of the two groups
γ refers to the clinically acceptable margin for non inferiority, equivalence or superiority
γ_0 represents a pre determined clinically acceptable margin
S^2 represents the pooled standard deviation of the comparison groups

*Non-inferiority design aims to prove that a novel treatment or intervention is not significantly inferior to an established standard treatment by a pre-determined margin.

**It states that within a pre-determined margin of difference, an equivalence design in RCT seeks to express that a novel treatment or intervention is equally effective to a recognized standard treatment.

***It is used when we need to demonstrate that the new therapy is more effective than currently available treatments or no treatment at all and in order to support regulatory approval of the new intervention and to direct clinical practice, superiority trial findings are used.

****it is a study designed in RCT where the mainaim is to expressthat one intervention is better than another in clinical outcomes.

We may have the response variable as binary variable and in such situations the sample size can be calculated for several response rates is presented in Table 3 by assuming some values of the parameters. However when the response variable is continuous in nature the sample size can be calculated for different response rates is presented in Table 4 for several population sizes.

Table 3: *Sample size calculations for different response rates when the outcome measure is a dichotomous variable*

t	$1-t$	t_0	$N1$	$N2$	$N3$	$N4$
0.4	0.6	0.58	82	105	143	607
0.45	0.55	0.6	85	108	232	626
0.47	0.53	0.63	86	109	220	630
0.48	0.52	0.66	86	109	184	632
0.49	0.51	0.68	86	109	173	632
0.52	0.48	0.7	86	109	208	632
0.54	0.46	0.72	85	108	220	629
0.57	0.43	0.75	84	107	240	620
0.59	0.41	0.79	83	105	211	612
0.9	0.1	0.8	31	39	1304	228

Table 4: *Sample size calculations for different response rates when the outcome measure is a continuous variable*

s^2	$N1$	$N2$	$N3$	$N4$
36	112	142	63	446
49	152	193	86	608
64	198	252	112	794
81	251	319	142	1004
100	310	393	175	1240
121	375	476	212	1500

Here,
t represents the response rate of the reference treatment group
t_0 denotes the response rate of the experimental group
S^2 represents the pooled standard deviation of the comparison groups
N_1 represents the sample size for the non inferiority study design
N_2 represents the sample size for the equivalence study design
N_3 represents the sample size for the statistical study design
N_4 represents the sample size for the clinical superiority study design

Helio Amante Miot [16] explained how to assessthe alpha level of the estimate, the utmostacceptable sample error (in units of the average value), and the population standard deviation of the quantitative variable (discrete or continuous) in order to characterize thepopulation estimates.One should ascertain the population frequency of the variable outcomes, the alpha level of the estimate, and the utmost acceptable sample error to characterize the population estimate represented by a categorical variable. Sample size considerations should be made for the percentage of each category that makes up a qualitative variable when it is not dichotomous. This subgroup's performance should be considered as the population estimate when the variable's population standard deviation or

frequency is unclear and the literature does not contain comparable data.A population's quantitative and qualitative characteristics can be described using formulas for sample sizing as

2.1 Quantitative variable

For infinite population,

$$n = \left(\frac{(Z_{\frac{\alpha}{2}}) \times \delta}{E} \right)^2 \tag{5}$$

For finite population,

$$n = \frac{N * \delta^2 * \left(Z_{\frac{\alpha}{2}} \right)^2}{(N-1) * E^2 + \left(\delta * Z_{\frac{\alpha}{2}} \right)^2} \tag{6}$$

where,
n = sample number
N = finite population size
δ = population standard deviation of the variable
$Z_{\frac{\alpha}{2}}$ = value of error α
E = standard error

2.2 Qualitative variable

For infinite population,

$$n = \left(\frac{(Z_{\frac{\alpha}{2}}) \times \sqrt{pq}}{E} \right)^2 \tag{7}$$

For finite population,

$$n = \frac{N * pq * \left(Z_{\frac{\alpha}{2}} \right)^2}{(N-1) * E^2 + pq \left(Z_{\frac{\alpha}{2}} \right)^2} \tag{8}$$

where,
p = ratio of desirable outcomes of the variable in a population
q = ratio of undesirable outcomes in a population

2.3 Formulae for sample sizing to evaluate two groups

The formulae for sample sizing to evaluate two groups based on quantitative and qualitative variables and according to the pairing of cases are obtained as

For Numeric variables: In case of independent sample, we have

$$n = (S_a^2 + S_b^2) * \left(\frac{Z_{\frac{\alpha}{2}} + Z_\beta}{d} \right)^2 \quad (9)$$

And for dependent sample,

$$nP = \left(\frac{Z_{\frac{\alpha}{2}} + Z_\beta * sd}{\overline{D}} \right) \quad (10)$$

Where,

Np = number of pairs

Z_β = value of error β

d = minimum difference between the average values

Sa^2 & Sb^2 = standard deviation of variable in each group

sd = standard deviation of dissimilarity within paired observations

$\overline{D}$ = average value of the dissimilarity with the paired observations

For Qualitative variable: In case of qualitative variable with non-paired sample,

$$n = (p_1 q_1 + p_2 q_2) * \left(\frac{Z_{\frac{\alpha}{2}} + Z_\beta}{p_1 - p_2} \right)^2 \quad (11)$$

And for paired sample we have,

$$nP = \left(\frac{Z_{\frac{\alpha}{2}} + 2Z_\beta * p_a * q_a}{4 * p_d * (p_a - 0.5)^2} \right)^2 \quad (12)$$

where,

p_1 and p_2 represents the ratio of desirable outcomes in subgroups 1 and 2 respectively

q_1 and q_2 represents the ratio of undesirable outcomes in subgroups 1 and 2 respectively

p_a = ratio of unrelated pairs of group 1

q_a = ratio of unrelated pairs of group 1

p_d = the two group's sum of the ratio of unrelated pairs

2.4 Quantitative variables with linear correlation

The sample-size formula for quantitative variables with linear correlation is given by

$$n = 4 + \left(\frac{Z_{\frac{\alpha}{2}} + Z_\beta}{0.5 * \ln\left(\frac{1+r}{1-r}\right)} \right)^2 \quad (13)$$

Where

r = represents the linear correlation coefficient

2.5 Sample size based on sensitivity and specificity

Zaidi *et al.* [40] have done a comprehensive study on estimating the sample size of diagnostic studies in health sciences and concluded that Sensitivity and specificity are two effective measures used in diagnostic testing and statistical analysis.

Sensitivity depicts a diagnostic test's capacity to accurately recognize people who have the condition it is planned to diagnose. In other words, it calculates the percentage of people who are truly positive for the disease out of all those who have the condition. A test with high sensitivity will have a low incidence of false negative results, making it unlikelythat those with the condition will go undiagnosed. A sensitivity rating of 100% would be ideal.

The capability of a diagnostic test to accurately identify individuals who do not possess the disease being tested for is measured by the term "specificity." In other terms, it counts the percentage of people who are truly negative about the condition. People who do not have the disease are unlikely to receive a false diagnosis when a test has a high specificity because of its low rate of false positives. A precision rating of 100% would be ideal.

The Various measures of diagnostic accuracy are

$$\text{Sensitivity} = \frac{(\text{True Positive})}{(\text{True Positive} + \text{False Negative})} * 100 \tag{14}$$

$$\text{Specificity} = \frac{(\text{True Negative})}{(\text{True Negative} + \text{False Positive})} * 100 \tag{15}$$

$$\text{Positive Predicative Values} = \frac{(\text{True Positive})}{(\text{True Positive} + \text{False Positive})} * 100 \tag{16}$$

$$\text{Negative Predicative Values} = \frac{(\text{True Negative})}{(\text{True Negative} + \text{False Negative})} * 100 \tag{17}$$

where,

True Positive (TP) cases are those where a test has accurately identified them as positive, indicating that the patient has the disease and the test has done its job.

The number of cases in which a test accurately identified them as negative while the patient did not have the disease is referred to as "True Negative" (TN).

False Positive (FP) cases are instances where a test result was incorrectly reported as positive even though the patient did not actually have the illness.

False Negative (FN) cases are those in which a test incorrectly reports a result as negative despite the fact that the patient actually has the illness.

The measurement of diagnostic effectiveness is given as

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \times 100 \tag{18}$$

In a particular population, prevalence denotes the count (percentage) of cases of disease present in that population. It is given by the following formula

$$P(\text{percentage}) = \frac{\text{Number of cases of disease}}{\text{Total number of Population}} \tag{19}$$

So, the formula for sensitivity and specificity of sample size are expressed as,

Based on sensitivity, sample size (n) is given by

$$n = \frac{Z^2_{1-\frac{\alpha}{2}} * S_N * (1 - S_N)}{L^2 * \text{Prevalence}} \tag{20}$$

Based on specificity, sample size (n) is given by

$$n = \frac{Z^2_{1-\frac{\alpha}{2}} * S_P * (1 - S_P)}{L^2 * (1 - \text{Prevalence})} \tag{21}$$

Where

$n = \text{requisite sample size}$

$S_N = \text{expected sensitivit y}$

$S_P = \text{expected specificit y}$

$\alpha = \text{Type1 error rate}$

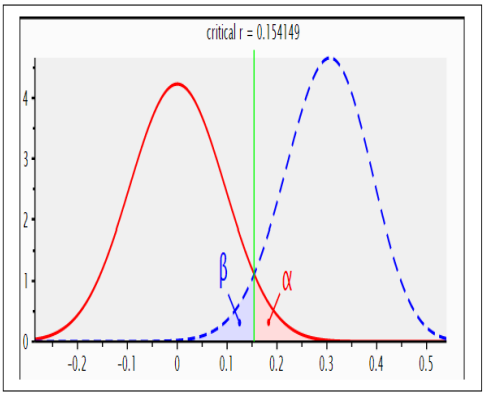
$Z_{1-\frac{\alpha}{2}} = \text{Normalized value}$

$L = \text{Exact accuracy}$

3. Graphical representation

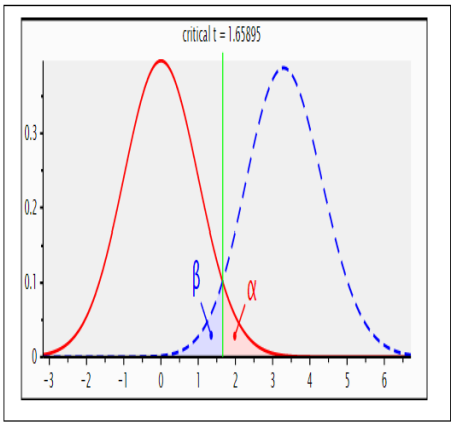
Incorporating the findings from our comparative analysis into the practical realm of clinical trials holds significant promise. Researchers and practitioners can leverage this knowledge to refine their study designs, ensuring that sample sizes align with research goals and statistical power requirements. Our research also emphasizes the importance of transparent reporting, promorting credibility in the scientific community. By embracing these applications, we can evaluate the quality of clinical trials and in turn, contribute to more reliable and valid research outcomes. Using the above several formulae in different circumstances we estimated the sample size using different parameters and the same has been presented in graphs as follows:

3.1 Correlation and Regression



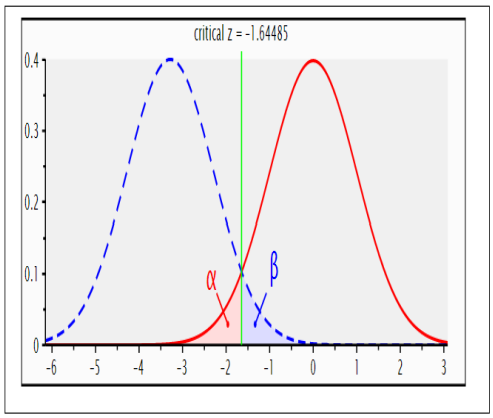
Input:	Tail(s)	=	One
	Correlation ρ H1	=	0.3
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Correlation ρ H0	=	0
Output:	Lower critical r	=	0.1541491
	Upper critical r	=	0.1541491
	Total sample size	=	115
	Actual power	=	0.9501151

Fig 1: *Correlation: Bivariate normal model for exact distribution*



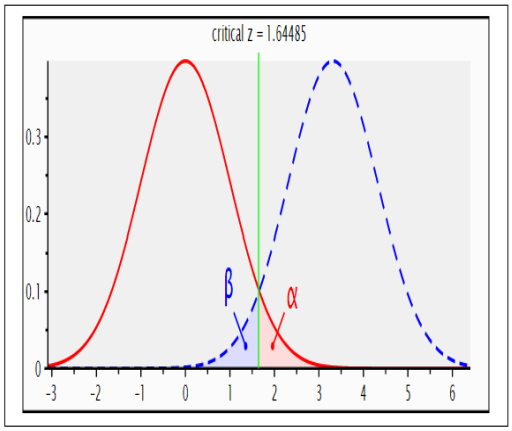
Input:	Tail(s)	=	One
	Effect size |ρ|	=	0.3
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
Output:	Non centrality parameter δ	=	3.3133098
	Critical t	=	1.6589535
	Df	=	109
	Total sample size	=	111
	Actual power	=	0.9503016

Fig 2: *t tests Correlation: Point biserial model*



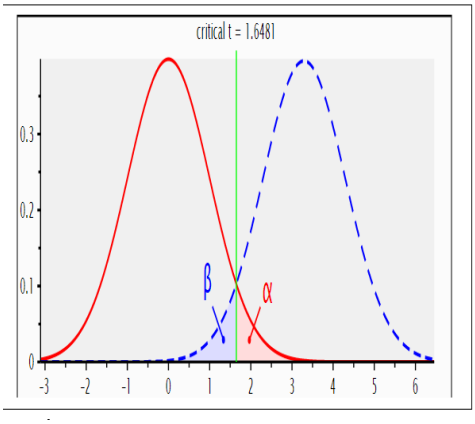
Input:	Tail(s)	=	One
	H1 corr ρ_ac	=	-0.1
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	H0 corr ρ_ab	=	0.1
	Corr ρ_bc	=	-0.1
Output:	Critical z	=	-1.6448536
	Sample size	=	595
	Actual power	=	0.9502184

Fig 3: *Z test correlations : Two dependent Pearson r's (common index)*



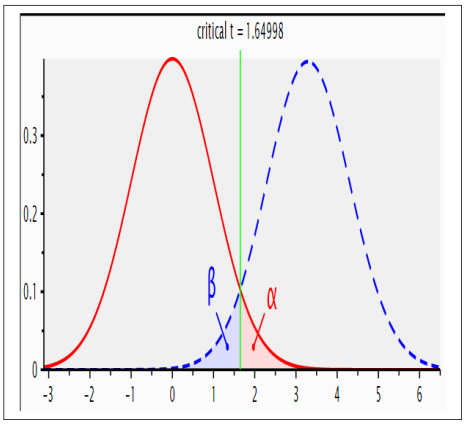
Input:	Tail(s)	=	One
	Effect size q	=	0.6
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Allocation ratio N2/N1	=	1
Output:	Critical z	=	1.6448536
	Sample size group 1	=	64
	Sample size group 2	=	64
	Total sample size	=	128
	Actual power	=	0.9524170

Fig 4: *Z test-Correlations: two independent Pearson r's*



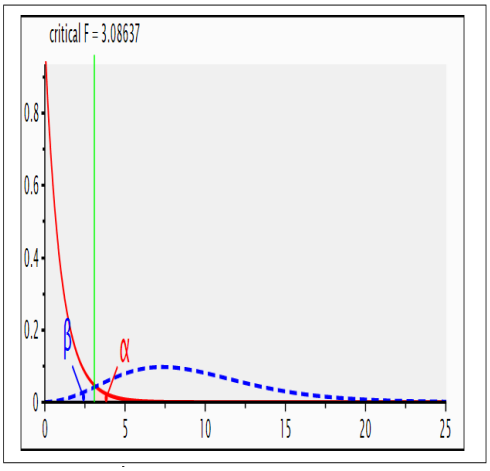
Input:	Tail(s)	=	One
	Slope H1	=	0.15
	α err prob	=	0.05
	Power (1−β err prob)	=	0.95
	Slope H0	=	0
	Std dev σx	=	1
	Std dev σy	=	1
Output:	Non centrality parameter δ	=	3.2961265
	Critical t	=	1.6481021
	Df	=	470
	Total sample size	=	472
	Actual power	=	0.9501720

Fig 5: *t tests-Linear bivariate regression: One group, size of slope*



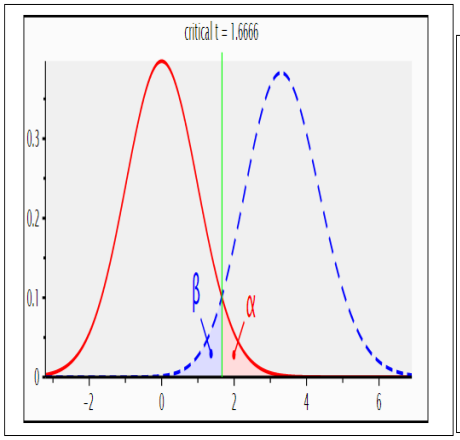
Input:	Tail(s)	=	One
	|Δ slope|	=	0.015
	α err prob	=	0.05
	Power (1−β err prob)	=	0.95
	Allocation ratio N2/N1	=	1
	Std dev residual σ	=	0.5
	Std dev σ_x1	=	20
	Std dev σ_x2	=	10
Output:	Non centrality parameter δ	=	3.2972716
	Critical t	=	1.6499830
	Df	=	298
	Sample size group 1	=	151
	Sample size group 2	=	151
	Total sample size	=	302
	Actual power	=	0.9500068

Fig 6: *t tests-Linear bivariate regression: two groups, difference between slopes*



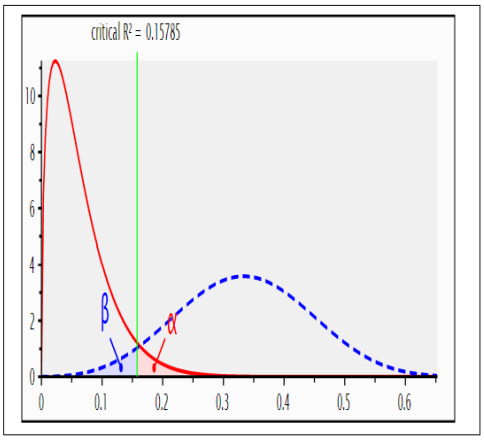
Input:	Effect size f^2	=	0.15
	α err prob	=	0.05
	Power (1−β err prob)	=	0.95
	Number of tested predictors	=	2
	Total number of predictors	=	5
Output:	Non centrality parameter λ	=	16.0500000
	Critical F	=	3.0863712
	Numerator df	=	2
	Denominator df	=	101
	Total sample size	=	107
	Actual power	=	0.9516875

Fig 7: *F tests-Linear multiple regression: Fixed model, R^2 increase*



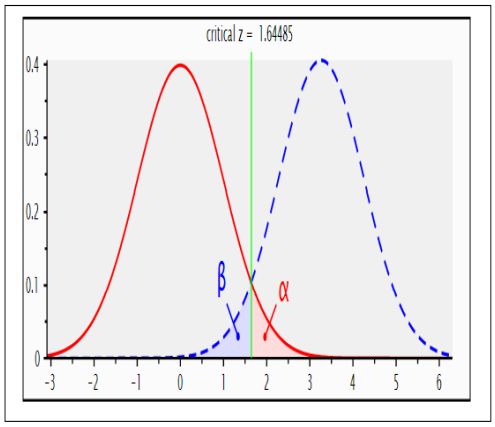
Input:	Tail(s)	= One
	Effect size f^2	= 0.15
	α err prob	= 0.05
	Power (1−β err prob)	= 0.95
	Number of predictors	= 2
Output:	Non centrality parameter δ	=3.3316662
	Critical t	=1.6665997
	Df	= 71
	Total sample size	= 74
	Actual power	=0.9510185

Fig 8: *t tests-Linear multiple regression: Fixed model, single regression coefficient*



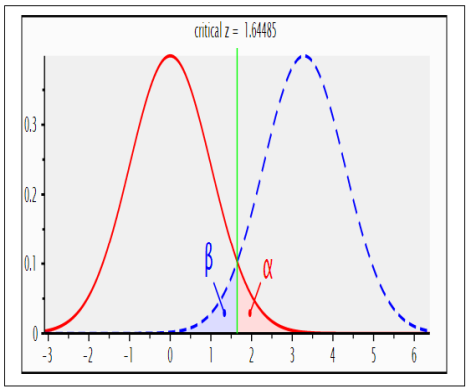
Input:	Tail(s)	= One
	H1 ρ^2	= 0.3
	H0 ρ^2	= 0
	α err prob	= 0.05
	Power (1−β err prob)	= 0.95
	Number of predictors	= 3
Output:	Lower critical R^2	=0.1578495
	Upper critical R^2	=0.1578495
	Total sample size	= 49
	Actual power	=0.9526746

Fig 9: *Exact-Linear multiple regression: Random model*



Input:	Tail(s)	= One
	Odds ratio	= 1.3
	Pr(Y=1|X=1) H0	= 0.2
	α err prob	= 0.05
	Power (1−β err prob)	= 0.95
	R^2 other X	= 0
	X distribution	= Normal
	X parm μ	= 0
	X parm σ	= 1
Output:	Critical z	=1.6448536
	Total sample size	= 988
	Actual power	=0.9501283

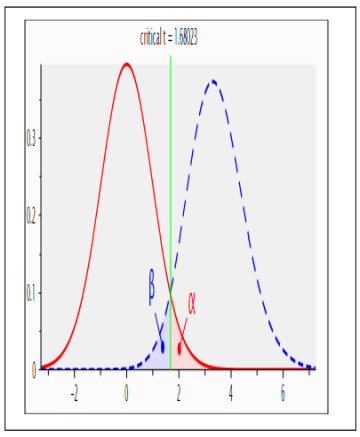
Fig 10: *Z tests-Logistic regression*



Input:	Tail(s)	=	One
	Exp(β1)	=	1.3
	α err prob	=	0.05
	Power (1−β err prob)	=	0.95
	Base rate exp(β0)	=	0.85
	Mean exposure	=	1
	R^2 other X	=	0
	X distribution	=	Normal
	X parm μ	=	0
	X parm σ	=	1
Output:	Critical z	=	1.6448536
	Total sample size	=	179
	Actual power	=	0.9502785

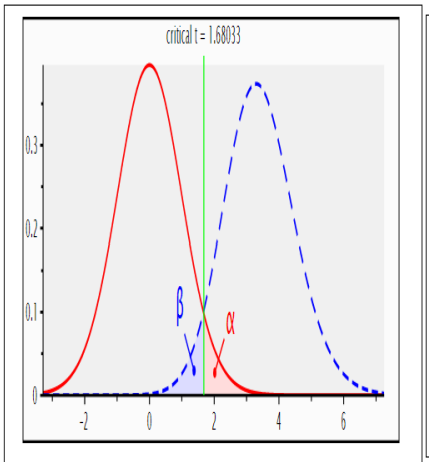
Fig 11: *Z tests-Poisson regression*

3.2 Means



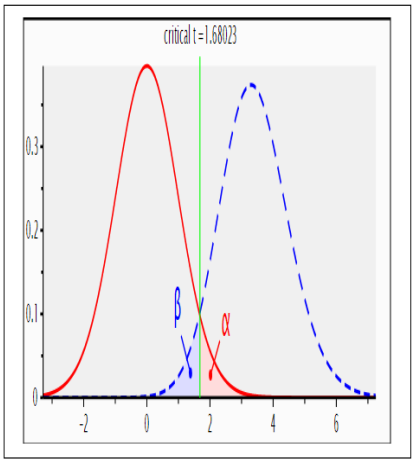
Input:	Tail(s)	=	One
	Effect size d	=	0.5
	α err prob	=	0.05
	Power (1−β err prob)	=	0.95
Output:	Non centrality parameter δ	=	3.3541020
	Critical t	=	1.6802300
	Df	=	44
	Total sample size	=	45
	Actual power	=	0.9512400

Fig 12: *t tests-Means: Difference from constant (One sample case)*



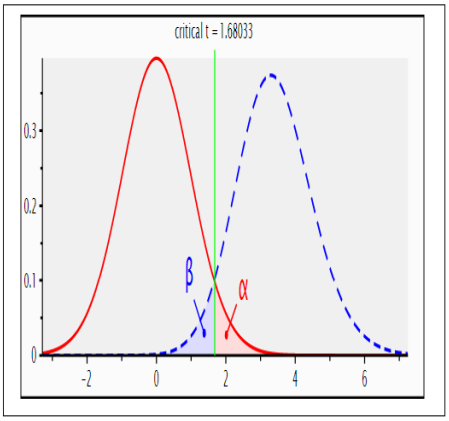
Input:	Tail(s)	=	One
	Parent distribution	=	Normal
	Effect size d	=	0.5
	α err prob	=	0.05
	Power (1−β err prob)	=	0.95
Output:	Non centrality parameter δ	=	3.3496901
	Critical t	=	1.6803274
	Df	=	43.8816940
	Total sample size	=	47
	Actual power	=	0.9507851

Fig 13: *t tests-Means: Wilcoxon signed-rank test (One sample case)*



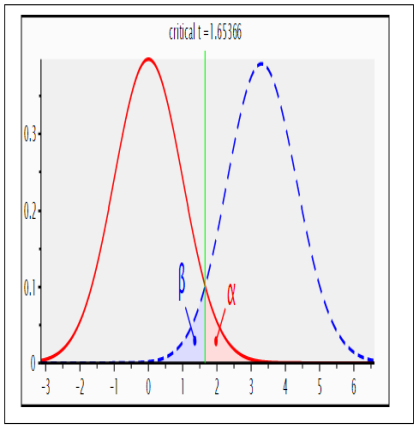
Input:	Tail(s)	=	One
	Effect size dz	=	0.5
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
Output:	Non centrality parameter δ	=	3.3541020
	Critical t	=	1.6802300
	Df	=	44
	Total sample size	=	45
	Actual power	=	0.9512400

Fig 14: *t tests-Means: Difference between two dependent means (matched pairs)*



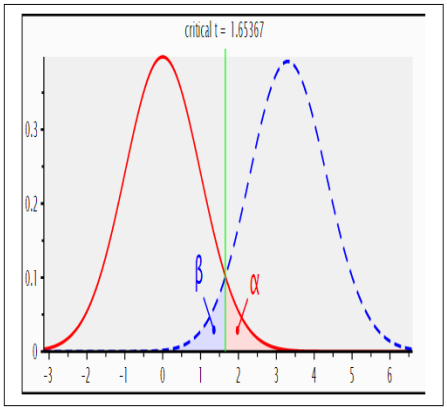
Input:	Tail(s)	=	One
	Parent distribution	=	Normal
	Effect size dz	=	0.5
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
Output:	Non centrality parameter δ	=	3.3496901
	Critical t	=	1.6803274
	Df	=	43.8816940
	Total sample size	=	47
	Actual power	=	0.9507851

Fig 15: *t tests-Means: Wilcoxon signed-rank test(matched pairs)*



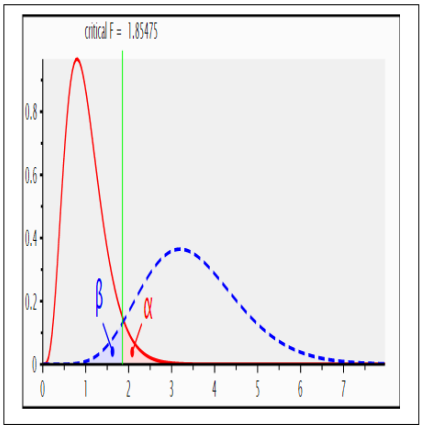
Input:	Tail(s)	=	One
	Effect size d	=	0.5
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Allocation ratio N2/N1	=	1
Output:	Non centrality parameter δ	=	3.3166248
	Critical t	=	1.6536580
	Df	=	174
	Sample size group 1	=	88
	Sample size group 2	=	88
	Total sample size	=	176
	Actual power	=	0.9514254

Fig 16: *t tests-Means: Difference between two independent means (two groups)*



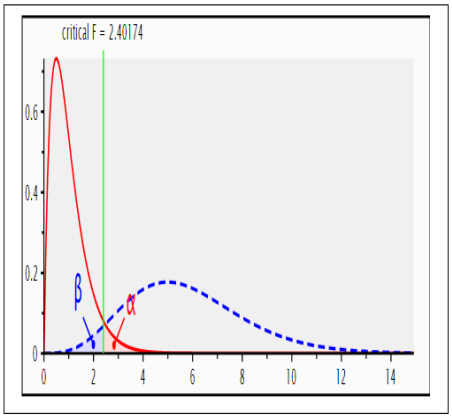
Input:	Tail(s)	=	One
	Parent distribution	=	Normal
	Effect size d	=	0.5
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Allocation ratio N2/N1	=	1
Output:	Non centrality parameter δ	=	3.3138635
	Critical t	=	1.6536729
	Df	=	173.7071
	Sample size group 1	=	92
	Sample size group 2	=	92
	Total sample size	=	184
	Actual power	=	0.9511454

Fig 17: *t tests-Means: Wilcoxon-Mann-Whitney test (two groups)*



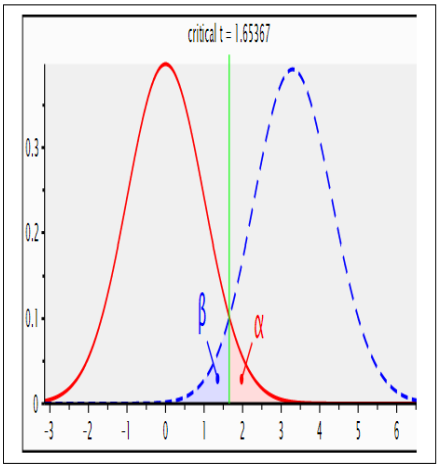
Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Numerator df	=	10
	Number of groups	=	5
	Number of covariates	=	1
Output:	Non centrality parameter λ	=	25.0000000
	Critical F	=	1.8547531
	Denominator df	=	394
	Total sample size	=	400
	Actual power	=	0.9504058

Fig 18: *F tests-ANCOVA: Fixed effects, main effects and interactions*



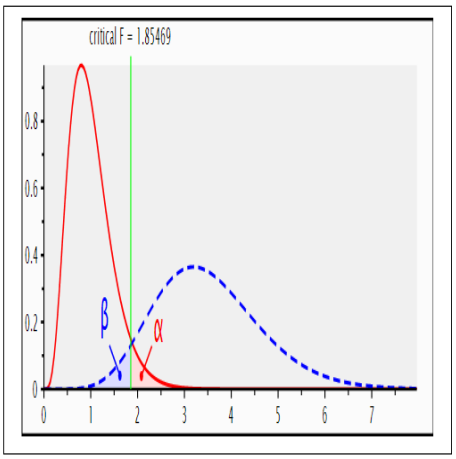
Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Number of groups	=	5
Output:	Non centrality parameter λ	=	19.0625000
	Critical F	=	2.4017397
	Numerator df	=	4
	Denominator df	=	300
	Total sample size	=	305
	Actual power	=	0.9521313

Fig 19: *F tests-ANOVA: Fixed effects, omnibus, one-way*



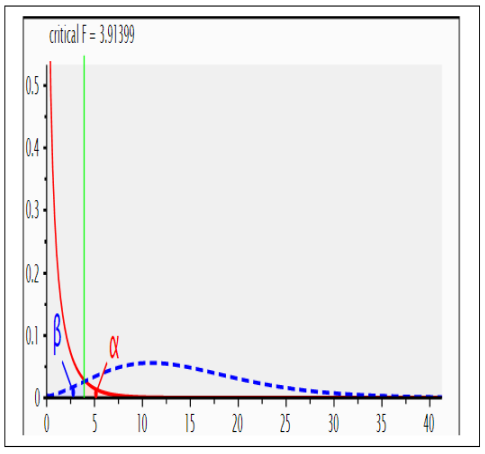
Input:	Tail(s)	=	One
	Parent distribution	=	Normal
	Effect size d	=	0.5
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Allocation ratio N2/N1	=	1
Output:	Non centrality parameter δ	=	3.3138635
	Critical t	=	1.6536729
	Df	=	173.7071
	Sample size group 1	=	92
	Sample size group 2	=	92
	Total sample size	=	184
	Actual power	=	0.9511454

Fig 20: *t tests-Means: Wilcoxon-Mann-Whitney test (two groups)*



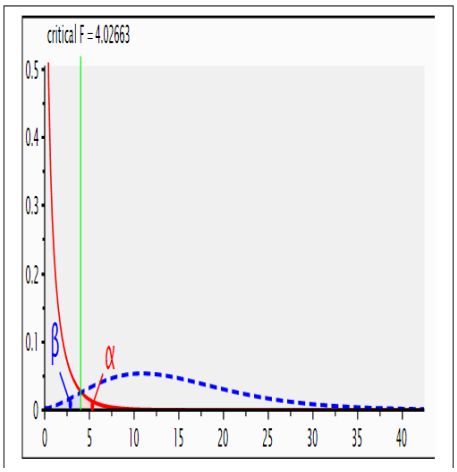
Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Numerator df	=	10
	Number of groups	=	5
Output:	Non centrality parameter λ	=	25.0000000
	Critical F	=	1.8546920
	Denominator df	=	395
	Total sample size	=	400
	Actual power	=	0.9504191

Fig 21: *F tests-ANOVA: Fixed effects, special, main effects and interactions*



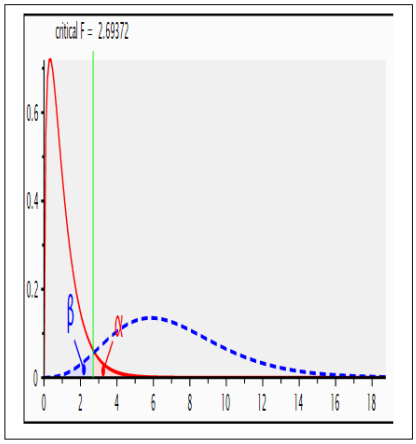
Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Number of groups	=	2
	Number of measurements	=	4
	Corr among rep measures	=	0.5
Output:	Noncentrality parameter λ	=	13.2000000
	Critical F	=	3.9139890
	Numerator df	=	1.0000000
	Denominator df	=	130
	Total sample size	=	132
	Actual power	=	0.9501436

Fig 22: *F tests-ANOVA: Repeated measures, between factors*



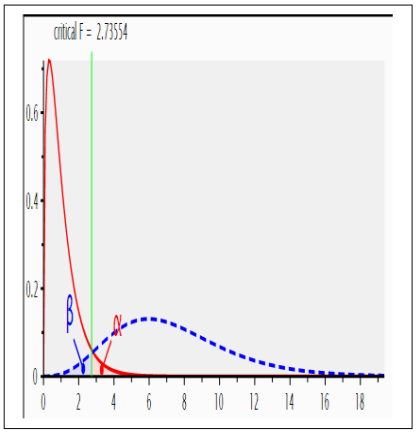
Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Number of groups	=	2
	Number of measurements	=	4
	Corr among rep measures	=	0
Output:	Noncentrality parameter λ	=	13.5000000
	Critical F	=	4.0266314
	Numerator df	=	1.0000000
	Denominator df	=	52.0000000
	Total sample size	=	54
	Actual power	=	0.9500773
	Pillai V	=	0.2000000

Fig 23: *F tests-MANOVA: Repeated measures, between factors*



Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Number of groups	=	2
	Number of measurements	=	4
	Corr among rep measures	=	0.5
	Non sphericity correction ϵ	=	1
Output:	Noncentrality parameter λ	=	18.0000000
	Critical F	=	2.6937209
	Numerator df	=	3.0000000
	Denominator df	=	102
	Total sample size	=	36
	Actual power	=	0.9517650

Fig 24: *F tests-ANOVA: Repeated measures, within factors*



Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1–β err prob)	=	0.95
	Number of groups	=	2
	Number of measurements	=	4
	Corr among rep measures	=	0
Output:	Noncentrality parameter λ	=	18.5000000
	Critical F	=	2.7355415
	Numerator df	=	3.0000000
	Denominator df	=	70.0000000
	Total sample size	=	74
	Actual power	=	0.9536728
	Pillai V	=	0.2000000

Fig 25: *F tests-MANOVA: Repeated measures, within factors*

The above sample size estimation in clinical trials has been done using different formulae at different situations and graphs have been drawn accordingly such as for correlation and regression, we need to know some given information such as level of significance, power of test and correlation coefficient under null and alternative hypothesis. Once the information is available we can substitute the available information in the formula and estimate the sample size along with actual power and lower

and upper critical value of correlation coefficient. Further, we can plot the same information in a graph such as given in Fig. 1 to Fig. 11. We can proceed in same passion for non-parametric tests too. The same can be concluded for Means, Proportions, Variance, and Generic etc. The Fig 1 to Fig. 11 presents the sample size estimation in graph for the data set concerning about the correlation and regression however if the concentration is on the mean the sample size graphs using the means are presented from Fig. 12 to 25 which is actually one of the mostly used statistic for the estimation of sample size. Thus, we can observe the behaviour of the sample size along with rest related parameters which is shows in the graphs from Fig. 1 to Fig. 25 for several characteristics of the study under consideration.

4. Conclusion

The comparative analysis of sample size determination procedures in clinical trials has shed light on the critical importance of this process in ensuring the reliability and validity of research results. It describes how choosing the right sample size based on the study's design and metrics may be done by researchers. It also offers advice on the data needed when requesting professional advice on evaluatingsample size in clinical trials. It is often recommended to presume that the sensitivity and specificity of the reference test are not exactly known when evaluating a novel diagnostic test. As a result, estimating them using the available methodologies is recommended. Unfortunately, sample size estimates for diagnostic investigations are infrequently disclosed by clinical investigators, and many doctors are ignorant of their significance. Instead, researchers frequently choose the sample size randomly, either out of convenience or in reliance on prior research. The precise interests of the researcher will ultimately determine the final sample size. Separate sample sizes should be chosen for each sensitivity and specificity if they are both equally crucial. The ultimate sample size would then be computed by selecting the greater of the two sample sizes. In instances where the researcher values sensitivity over specificity, the sample size would be determined solely by sensitivity. It is standard procedure for researchers to raise the sample size by 10% for the sake of accommodating people whoareunreachable.

Furthermore, the sample size is frequently raised by 30% to account for non-response. In order to get the appropriate degree of confidence and precision, more surveys or scheduled interviews may be conducted than is necessary. It follows that the determination of sample size in clinical trialsdepends upon the issue being addressed.

Ultimately, this research serves as a call to action for researchers, clinicians and educators alike. It emphasizes the imperative of elevating the discourse on sample size determination, promoting transparency and enhancing the quality of clinical trials to ensure that the research outcomes we generate can be trusted and applied to improve patient care and advance medical knowledge.

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