



The
University
Of
Sheffield.

SCHOOL OF MATHEMATICS AND STATISTICS

Spring Semester 2018–2019

Sampling, Design, Medical Statistics

3 hours

*Candidates may bring to the examination a calculator that conforms to University regulations. All answers will be marked but credit will be given only for the best **FIVE** answers. All questions are worth 20 marks. Total marks 100.*

Please leave this exam paper on your desk
Do not remove it from the hall

Registration number from U-Card (9 digits)
to be completed by student

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- 1 A clinician investigating treatments for Parkinson’s disease conducts a small, double blind, crossover trial of a promising new drug against a placebo. Patients were allocated at random to either Group 1 or Group 2, where Group 1 received the treatments in the order Drug then Placebo, while Group 2 received first Placebo then Drug. The first treatment was applied for 4 weeks (Period 1), then patients swapped to their second treatment for a further 4 weeks (Period 2). A score was given for each period based on average symptom severity over the 4 weeks (low values are good). The results are given below:

Group	Patient	Period 1 Score	Period 2 Score
Group 1	1	8.75	8.75
Drug → Placebo	2	10.50	9.75
	3	15.00	18.50
	4	21.00	21.50
Group 2	5	22.00	18.00
Placebo → Drug	6	15.00	13.00
	7	14.00	13.75
	8	22.75	21.50

- (i) Explain what is meant by a ‘double blind’ trial and why they are used. **(2 marks)**
- (ii) Assuming each group’s data is Normally distributed and that there is no carryover effect from Period 1 to Period 2,
- (a) assess whether there is a statistically significant treatment effect. **(7 marks)**
- (b) provide an estimate of the drug’s effect. **(3 marks)**
- (iii) For each of the assumptions stated in (ii), explain how you could test whether the assumption held and how you would proceed if it were violated. [You do not need to carry out any of the analyses you suggest.] **(4 marks)**
- (iv) Give two reasons why it is considered important to minimize sample sizes in clinical trials. **(2 marks)**
- (v) Crossover trials are typically used, because they are more efficient than a similarly-sized parallel group study due to the correlation between observations made on the same patient. If this study is as efficient as a study using a total of 24 patients in 2 (equal) parallel groups, how large is the correlation between Period 1 and 2 observations on a single patient? **(2 marks)**

- 2 (i) Which of the following trial designs:
- 2-period, 2-treatment crossover
 - sequential
 - parallel group
 - factorial

would be most appropriate for investigating the relative benefits of 'stomach stapling surgery' and 'support from a dietician' in treatment of obesity? Explain your reasoning. **(4 marks)**

- (ii) A study has been conducted to compare a RAST (radioallergosorbent) test and a new, simpler, cheaper multi-RAST, or MAST, test of allergy. The data are categorized test responses and given in the following table:

		RAST					Total
		Negative	Weak	Moderate	High	Very high	
MAST	Negative	86	3	14	0	2	105
	Weak	26	0	10	4	0	40
	Moderate	20	2	22	4	1	49
	High	11	1	37	16	14	79
	Very high	3	0	15	24	48	90
Total		146	6	98	48	65	363

By calculating the κ statistic, assess how well the MAST test agrees with the RAST test. **(6 marks)**

- (iii) 21 patients with acute myeloid leukemia were randomised to one of two forms of treatment and followed up until death. The data below show the times until death in months. 6 patients were lost to follow up before death was observed, these censored observation are denoted by asterisks in the table.

Treatment	Remission/Censored Times (months)											Total Time in Study
	1*	1	3	6	7	13*	18	20	28	35		
New												132
Standard	1	2*	5	10*	11	12	21	26*	43	46*	52	229

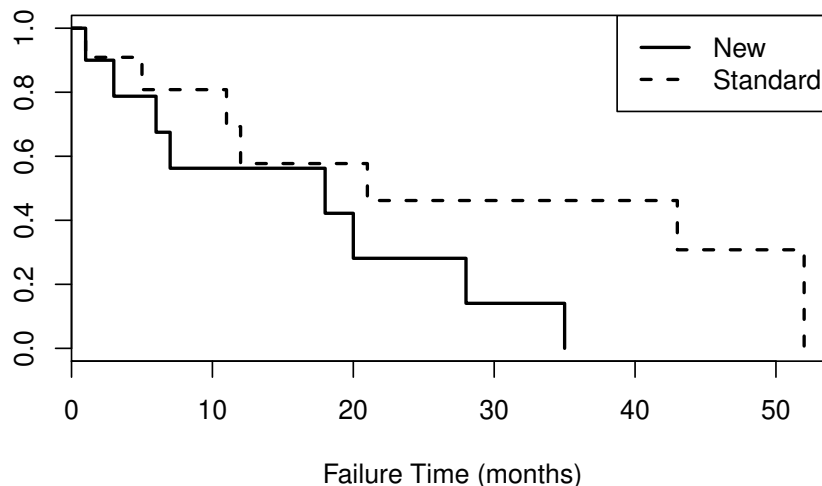
2 (continued)

Given below are the results of a Kaplan-Meier preliminary graphical analysis of the data

```
> Leuk.sv <- Surv(Time, Status, type = "right")
> # Find KM estimate
> KMest <- survfit(Leuk.sv ~ type)
> summary(KMest)
Call: survfit(formula = Leuk.sv ~ type)
```

type=New							
time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI	95% CI
1	10	1	0.900	0.0949	0.7320	1.000	
3	8	1	0.787	0.1340	0.5641	1.000	
6	7	1	0.675	0.1551	0.4303	1.000	
7	6	1	0.562	0.1651	0.3165	1.000	
18	4	1	0.422	0.1737	0.1883	0.945	
20	3	1	0.281	0.1631	0.0903	0.876	
28	2	1	0.141	0.1286	0.0234	0.844	
35	1	1	0.000	NaN	NA	NA	

type=Standard							
time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI	95% CI
1	11	1	0.909	0.0867	0.754	1.000	
5	9	1	0.808	0.1225	0.600	1.000	
11	7	1	0.693	0.1498	0.453	1.000	
12	6	1	0.577	0.1634	0.331	1.000	
21	5	1	0.462	0.1666	0.228	0.936	
43	3	1	0.308	0.1677	0.106	0.895	
52	1	1	0.000	NaN	NA	NA	



2 (continued)

- (a) Without making any model assumptions, estimate the median failure times for the two treatments. **(2 marks)**
- (b) It is suggested that the survival times for the two treatments are Exponentially distributed with rates λ_A and λ_B respectively. Under this assumption:
- (α) Estimate the mean failure times with approximate 95% confidence intervals. **(3 marks)**
- (β) Use the likelihood ratio test to assess whether there is a difference in the failure time distribution of the two components. **(3 marks)**
- (c) If it was known that the censored patients had in fact been moved to a hospice for end-of-life care how might this affect the suitability of the analysis suggested above? **(2 marks)**

- 3 (i) In a study for an engineering company, 100 drill batteries were constructed and then randomised to two different test environments — use on wood and use on brick. Time until the battery ran out was studied as the survival time of interest. Drills still operating at the conclusion of the study were considered right-censored. The data are stored in `drill` and coding for the different variables is shown below.

Coding:

env: test environment (0 = wood; 1 = brick)

time: battery life in hours

status: indicator of failure (1) or censoring (0)

Some R analysis was performed with the output shown below:

```
> fit <- survreg(Surv(time, status) ~ env, data=drill,
+ dist="exponential")
> summary(fit)
```

Call:

```
survreg(formula = Surv(time, status) ~ env, data = drill,
+ dist = "exponential")
```

	Value	Std. Error	z	p
(Intercept)	-1.327	0.141	-9.38	<2e-16
env	0.405	0.200	2.02	0.043

Scale fixed at 1

Exponential distribution

Loglik(model)= 12.5 Loglik(intercept only)= 10.4

Chisq= 4.07 on 1 degrees of freedom, p= 0.044

Number of Newton-Raphson Iterations: 4

n= 100

- (a) Describe the analysis performed and the final model for T , the battery life, for both the wood and brick test environments. *(4 marks)*
- (b) Is there evidence that the test environment makes a difference to battery life? Does the battery last longer when used on wood or brick? *(2 marks)*
- (c) Estimate the mean battery life for a drill used on wood; and separately used on brick. *(2 marks)*

3(continued)

- (ii) A cohort study to investigate diet was carried out on a group of men. Before entering the study each individual was asked for their smoking and drinking habits; and whether they were vegetarian or not. Their weights were also recorded (kg) and centred around 75 kg (i.e. 85 would be coded as 10 and 70 as -5). The outcome of interest was all-cause mortality. A Cox proportional hazards model was fitted to the data and the output is shown below:

Variable	Coefficient	Standard Error
Smoking Habits		
Smoker	Reference	—
Non-smoker	-0.25	0.03
Drinking Status		
Regular Drinker	Reference	—
Occasional Drinker	-0.15	0.34
Never Drink	-0.33	0.08
Weight (centred on 75 kgs as baseline)	0.0004	0.0001
Vegetarian		
Yes	Reference	—
No	-0.32	0.31

Table: Log hazard ratio of mortality with standard errors

- (a) Write down the model fitted. **(4 marks)**
- (b) Describe in detail the effects of these variables on survival. **(5 marks)**
- (c) Using the model, calculate the estimate of the hazard ratio comparing
- A smoker weighing 83kg who denotes themselves as regular drinker and who **is** a vegetarian;
 - A non-smoker weighing 71kg who denotes themselves as a non-drinker and who **is not** a vegetarian.

(3 marks)

- 4 An investigator is studying the dependence of a variable Y on one continuous explanatory variable x which has been scaled to lie between -1 and 1 . It is assumed that $E(Y) = 0$ when $x = 0$, and the following model (model 1) is proposed.

$$\text{model 1 : } E(Y) = \beta_1 x + \beta_{11} x^2.$$

The investigator proposes the following design (design A) using four observations:

Design	Design points (x)
A	$\{-1, 0, 0, 1\}$

- (i) Explain why β_1 and β_{11} in Model 1 are orthogonal to each other in design A. **(3 marks)**
- (ii) The investigator thinks that collecting further observations at $x = 0$ would reduce the prediction variance for all x satisfying $-1 \leq x \leq 1$ for design A in model 1. Justify whether they are correct or not. **(3 marks)**
- (iii) For model 1, specify the design using four observations that has β_1 orthogonal to β_{11} and that minimises the variance of $\hat{\beta}_{11}$. Justify your answer. **(5 marks)**
- (iv) Suppose instead the investigator proposes the following model (model 2)

$$\text{model 2 : } E(Y) = \beta_1 x + \beta_{11} x^2 + \beta_{111} x^3.$$

Justify whether design A is a suitable design for model 2. **(2 marks)**

- (v) The investigator now believes an intercept is needed and proposes another new model (model 3)

$$\text{model 3 : } E(Y) = \beta + \beta_1 x + \beta_{11} x^2.$$

Justify whether design A is G -optimal for model 3. You may find the following result useful

$$\begin{pmatrix} 2 & 0 & 1 \\ 0 & 1 & 0 \\ 1 & 0 & 1 \end{pmatrix} \begin{pmatrix} 1 & 0 & -1 \\ 0 & 1 & 0 \\ -1 & 0 & 2 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}.$$

(7 marks)

- 5 Throughout this question assume that all four variables (x_1, x_2, x_3, x_4) are factors occurring at two levels, denoted +1 and -1.
- (i) Suppose that four design points are available in a fractional factorial design. Specify two design generators that allow the intercept and the main effects for x_1, x_2 and x_3 to be included in a linear model without confounding. Show the alias structure for these two generators (you can leave the alias structure in terms of x_1, x_2, x_3 and x_4 rather than in terms of $\beta_1, \beta_2, \dots, \beta_{1234}$). **(3 marks)**
 - (ii) Construct the fractional factorial design using your design in part (i). **(3 marks)**
 - (iii) Consider a screening experiment with four variables x_1, x_2, x_3, x_4 . If the interest is only in the main effects of x_1, x_2, x_3 and x_4 , construct a design suitable for a screening experiment using eight observations. **(5 marks)**
 - (iv) Write down a Latin square that could be used as a design with 16 observations for an experiment with three factor variables each taking four levels. **(2 marks)**
 - (v) Suppose the investigator also wants to include a blocking factor with four levels into the design in part (iv). Describe how this could be done still using 16 observations. **(3 marks)**
 - (vi) Write down the linear model that could be used with the design in part (v), define all notation and specify all constraints. **(4 marks)**

- 6 A small survey has been conducted to estimate the proportion of the population in favour of lowering the retirement age. The sample was drawn using simple random sampling. The sex of each participant in the survey was also recorded, and the results are given below.

	males	females
in favour	23	15
against	18	44

- (i) Estimate the population proportion in favour of lowering the retirement age using the simple random sampling estimator. **(2 marks)**
- (ii) Assume that half the population are female. Estimate the population proportion in favour of lowering the retirement age using an alternative estimator that makes use of the assumed proportion of females in the population. **(2 marks)**
- (iii) An opinion poll is to be conducted to estimate the proportion of voters who intend to vote for the Liberal Democrats at the next UK General Election. If a simple random sample is to be used, how large would the sample need to be to ensure that a 99% confidence interval for the true proportion was no wider than 0.05. You may ignore the finite population correction. **(5 marks)**
- (iv) For your choice of n in part (iii), would you expect the observed 99% confidence interval to be narrower than 0.05? Explain your answer. **(3 marks)**
- (v) Discuss briefly when cluster sampling might give a less accurate estimator of the population mean than using simple random sampling (drawing a diagram here might be helpful). **(3 marks)**
- (vi) In cluster sampling that we studied, the cluster sizes are assumed to be equal to each other. Suppose instead that this is no longer true. Specifically, suppose that there are three clusters of sizes k_1 , k_2 and k_3 where it is not true that $k_1 = k_2 = k_3$. Consider an estimator that is the sample mean of two randomly selected clusters (assume that you still measure all units in the selected clusters). Justify whether this is an unbiased estimator of the population mean. **(5 marks)**

End of Question Paper

MAS6012 FORMULA SHEET & CRITICAL VALUES

1 Clinical Trials Formulae

Two Sample t-Test — Separate variances form $r = \min(n_1, n_2)$

$$t_r = \left| \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{S_1^2}{n_1} + \frac{S_2^2}{n_2}}} \right|$$

Two Sample t-Test — Pooled variance form $r = n_1 + n_2 - 2$

$$t_r = \left| \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{(n_1-1)S_1^2 + (n_2-1)S_2^2}{n_1+n_2-2} \left(\frac{1}{n_1} + \frac{1}{n_2}\right)}} \right|$$

Sample Size Calculations — Two sample test for proportions NB number in each group

$$n \simeq \frac{\theta_2(1-\theta_2) + \theta_1(1-\theta_1)}{(\theta_2 - \theta_1)^2} [\Phi^{-1}(\beta) + \Phi^{-1}(\alpha/2)]^2$$

Sample Size Calculations — Two sample test for means NB number in each group

$$n \simeq \frac{2\sigma^2}{(\mu_2 - \mu_1)^2} [\Phi^{-1}(\beta) + \Phi^{-1}(\alpha/2)]^2$$

Standard Error for Natural Logarithm of Relative Risk

$$s.e.[(\log_e(RR))] = \sqrt{\frac{1}{a} - \frac{1}{a+b} + \frac{1}{c} - \frac{1}{c+d}}$$

Standard Error for Natural Logarithm of Odds Ratio

$$s.e.[(\log_e(OR))] = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$$

2 Survival Analysis Formulae

Exponential Distributions — MLE of rate λ with censoring The mle

$$\hat{\lambda} = \frac{\sum_{i=1}^n \delta_i}{\sum_{i=1}^n t_i} = \frac{\Delta}{T} \quad \text{var}(\hat{\lambda}) \approx \frac{\hat{\lambda}^2}{\sum_{i=1}^n \delta_i}$$

For any (differentiable, monotonic) function $g(\cdot)$,

$$\text{var}(g(\hat{\lambda})) \approx [g'(\lambda)]^2 \text{var}(\lambda)_{\lambda=\hat{\lambda}}$$

so e.g.

$$\text{var}\left(\frac{1}{\hat{\lambda}}\right) = \text{var}(\hat{\mu}) \approx \frac{\hat{\mu}^2}{\sum_{i=1}^n \delta_i}$$

Exponential Distributions — MLE test

$$W = \frac{\hat{\lambda}_1 - \hat{\lambda}_2}{\sqrt{\frac{\hat{\lambda}_1^2}{\Delta_1} + \frac{\hat{\lambda}_2^2}{\Delta_2}}} \approx N(0, 1)$$

Exponential Distributions — LRT test

$$2 \left\{ \Delta_1 \log \frac{\Delta_1}{T_1} + \Delta_2 \log \frac{\Delta_2}{T_2} - (\Delta_1 + \Delta_2) \log \frac{\Delta_1 + \Delta_2}{T_1 + T_2} \right\} \approx \chi_1^2$$

Log-rank Statistic

$$LR = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} \sim \chi_1^2$$

3 Design Formulae

Linear Model formulae

$$\hat{\beta} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \mathbf{Y} \quad \text{and} \quad \hat{\beta} \sim N\{\beta, \sigma^2 (\mathbf{X}^T \mathbf{X})^{-1}\}$$

Prediction Variance

$$\text{var } \hat{y}(\mathbf{x}_0) = \sigma^2 \mathbf{f}(\mathbf{x}_0)^T (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{f}(\mathbf{x}_0)$$

Standardized Prediction Variance

$$d(\mathbf{x}) = n \mathbf{f}(\mathbf{x})^T (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{f}(\mathbf{x}) = \mathbf{f}(\mathbf{x})^T \mathbf{M}^{-1} \mathbf{f}(\mathbf{x})$$

Confidence Regions, σ^2 unknown

$$p^{-1} \hat{\sigma}^{-2} (\hat{\beta} - \beta)^T \mathbf{X}^T \mathbf{X} (\hat{\beta} - \beta) \text{ has an } F_{p, n-p} \text{ distribution, provided } n > p$$

Balanced Incomplete Block Design Notation

- t = number of treatments
- k = number of units in a block
- b = number of blocks
- r = number of applications of each treatment
- λ = number of times each pair of treatments appears together in a block

Balanced Incomplete Block Design Relationships

$$\begin{aligned} t &> k \\ bk &= rt \\ r(k-1) &= \lambda(t-1) \end{aligned}$$

Balanced Incomplete Block Design - Unreduced Design

$$b = \binom{t}{k} \quad r = \binom{t-1}{k-1} \quad \lambda = \binom{t-2}{k-2}$$

Efficiency of Balanced Incomplete Block Design compared to a Randomized Block design

$$\frac{1 - t^{-1}}{1 - k^{-1}}$$

Adding an extra point \mathbf{x}

$$|\mathbf{G}^*| = |\mathbf{G}| (1 + \mathbf{f}(\mathbf{x})^T \mathbf{G}^{-1} \mathbf{f}(\mathbf{x}))$$

Deleting an existing point \mathbf{x}

$$|\mathbf{G}^*| = |\mathbf{G}| (1 - \mathbf{f}(\mathbf{x})^T \mathbf{G}^{-1} \mathbf{f}(\mathbf{x}))$$

Adding a new point \mathbf{y} and deleting an existing point \mathbf{x}

$$|\mathbf{G}_2| = |\mathbf{G}| \left\{ (1 - \mathbf{f}(\mathbf{x})^T \mathbf{G}^{-1} \mathbf{f}(\mathbf{x})) (1 + \mathbf{f}(\mathbf{y})^T \mathbf{G}^{-1} \mathbf{f}(\mathbf{y})) + (\mathbf{f}(\mathbf{x})^T \mathbf{G}^{-1} \mathbf{f}(\mathbf{y}))^2 \right\}$$

4 Sample Surveys and Computer Experiments Formulae

Population variance

$$S^2 = \frac{1}{N-1} \sum_1^N (X_i - \bar{X})^2 = \frac{1}{N-1} \left(\sum_{i=1}^N X_i^2 - N \bar{X}^2 \right)$$

and for a binary characteristic ($X_i = 1$ or 0 for each i),

$$S^2 = \frac{NP(1-P)}{N-1}$$

Variance of sample mean for simple random sampling

$$\text{var } \bar{x} = \left(1 - \frac{n}{N}\right) \frac{S^2}{n}.$$

Sample size to achieve given confidence interval width for simple random sampling

$$n \geq \frac{N}{1 + N(d/(2Sz_{\alpha/2}))^2}$$

Stratified estimate of population mean and its variance

$$\bar{x}_{st} = \frac{1}{N} \sum_1^l N_i \bar{x}_i \quad \text{and} \quad \text{var } \bar{x}_{st} = \sum_1^l \left(\frac{N_i}{N}\right)^2 \frac{1-f_i}{n_i} S_i^2.$$

Allocation methods

$$\text{Optimal allocation: } n_i \propto \frac{N_i S_i}{\sqrt{c_i}} \quad \text{Neyman allocation: } n_i = \frac{n N_i S_i}{\sum_1^l N_i S_i}$$

Cluster estimate of population mean and its variance

$$\bar{x}_{cl} = \frac{1}{lK} \sum_1^l \sum_1^K x_{ij} \quad \text{and} \quad \text{var } (\bar{x}_{cl}) = \frac{1-f}{l} \frac{1}{L-1} \sum_1^L (\bar{X}_i - \bar{X})^2$$

Regression estimator of population mean and its variance

$$\bar{x}_{lr} = \bar{x} - \hat{\beta}(\bar{y} - \bar{Y}) \quad \text{and} \quad \text{var } \bar{x}_{lr} \simeq \frac{1-f}{n} S_X^2 (1 - \rho^2)$$

Approximate variance of the Peterson estimator, Chapman estimator and approximate variance

n : size of 1st sample, m : size of 2nd sample.

$$\begin{aligned} \widehat{Var}(\hat{N}_p) &= \frac{mn^2(m-r)}{r^3}, \\ \hat{N}_c &= \frac{(n+1)(m+1)}{r+1} - 1, \\ \widehat{Var}(\hat{N}_c) &= \frac{(n+1)(m+1)(n-r)(m-r)}{(r+1)^2(r+2)}. \end{aligned}$$

Variance identity

$$\text{Var}(Y) = \text{Var}_X\{E(Y|X)\} + E_X\{\text{Var}(Y|X)\}.$$

5 Tables of Percentage Points (also known as Quantiles or Critical Values) for Three Standard Distributions

The tables contain values of quantiles q such that $P[X \leq q] = p$ for various probabilities p when X has the specified distribution (which may depend on particular degrees of freedom ν). In these tables, p has been expressed as a percentage rather than a decimal. The relevant R commands for generating the q are also shown. For the $N(0, 1)$ distribution, the tabulated function is also known as the Φ^{-1} function.

STANDARD NORMAL DISTRIBUTION PERCENTAGE POINTS

qnorm(p) where p is percentage, e.g. for 95%, $p = 0.95$

	60.0%	66.7%	75.0%	80.0%	87.5%	90.0%	95.0%	97.5%	99.0%	99.5%	99.9%
qnorm	0.253	0.431	0.674	0.842	1.150	1.282	1.645	1.960	2.326	2.576	3.090

CHI-SQUARED PERCENTAGE POINTS

qchisq(p, ν) where p is percentage, e.g. for 95%, $p = 0.95$

ν	60.0%	66.7%	75.0%	80.0%	87.5%	90.0%	95.0%	97.5%	99.0%	99.5%	99.9%
1	0.708	0.936	1.323	1.642	2.354	2.706	3.841	5.024	6.635	7.879	10.828
2	1.833	2.197	2.773	3.219	4.159	4.605	5.991	7.378	9.210	10.597	13.816
3	2.946	3.405	4.108	4.642	5.739	6.251	7.815	9.348	11.345	12.838	16.266
4	4.045	4.579	5.385	5.989	7.214	7.779	9.488	11.143	13.277	14.860	18.467
5	5.132	5.730	6.626	7.289	8.625	9.236	11.070	12.833	15.086	16.750	20.515
6	6.211	6.867	7.841	8.558	9.992	10.645	12.592	14.449	16.812	18.548	22.458
7	7.283	7.992	9.037	9.803	11.326	12.017	14.067	16.013	18.475	20.278	24.322
8	8.351	9.107	10.219	11.030	12.636	13.362	15.507	17.535	20.090	21.955	26.125
9	9.414	10.215	11.389	12.242	13.926	14.684	16.919	19.023	21.666	23.589	27.877
10	10.473	11.317	12.549	13.442	15.198	15.987	18.307	20.483	23.209	25.188	29.588

STUDENT'S t PERCENTAGE POINTS

qt(p, ν) where p is percentage, e.g. for 95%, $p = 0.95$

ν	60.0%	66.7%	75.0%	80.0%	87.5%	90.0%	95.0%	97.5%	99.0%	99.5%	99.9%
1	0.325	0.577	1.000	1.376	2.414	3.078	6.314	12.706	31.821	63.657	318.31
2	0.289	0.500	0.816	1.061	1.604	1.886	2.920	4.303	6.965	9.925	22.327
3	0.277	0.476	0.765	0.978	1.423	1.638	2.353	3.182	4.541	5.841	10.215
4	0.271	0.464	0.741	0.941	1.344	1.533	2.132	2.776	3.747	4.604	7.173
5	0.267	0.457	0.727	0.920	1.301	1.476	2.015	2.571	3.365	4.032	5.893
6	0.265	0.453	0.718	0.906	1.273	1.440	1.943	2.447	3.143	3.707	5.208
7	0.263	0.449	0.711	0.896	1.254	1.415	1.895	2.365	2.998	3.499	4.785
8	0.262	0.447	0.706	0.889	1.240	1.397	1.860	2.306	2.896	3.355	4.501
9	0.261	0.445	0.703	0.883	1.230	1.383	1.833	2.262	2.821	3.250	4.297
10	0.260	0.444	0.700	0.879	1.221	1.372	1.812	2.228	2.764	3.169	4.144
11	0.260	0.443	0.697	0.876	1.214	1.363	1.796	2.201	2.718	3.106	4.025
12	0.259	0.442	0.695	0.873	1.209	1.356	1.782	2.179	2.681	3.055	3.930
13	0.259	0.441	0.694	0.870	1.204	1.350	1.771	2.160	2.650	3.012	3.852
14	0.258	0.440	0.692	0.868	1.200	1.345	1.761	2.145	2.624	2.977	3.787
15	0.258	0.439	0.691	0.866	1.197	1.341	1.753	2.131	2.602	2.947	3.733
16	0.258	0.439	0.690	0.865	1.194	1.337	1.746	2.120	2.583	2.921	3.686
17	0.257	0.438	0.689	0.863	1.191	1.333	1.740	2.110	2.567	2.898	3.646
18	0.257	0.438	0.688	0.862	1.189	1.330	1.734	2.101	2.552	2.878	3.610
19	0.257	0.438	0.688	0.861	1.187	1.328	1.729	2.093	2.539	2.861	3.579
20	0.257	0.437	0.687	0.860	1.185	1.325	1.725	2.086	2.528	2.845	3.552
21	0.257	0.437	0.686	0.859	1.183	1.323	1.721	2.080	2.518	2.831	3.527
22	0.256	0.437	0.686	0.858	1.182	1.321	1.717	2.074	2.508	2.819	3.505
23	0.256	0.436	0.685	0.858	1.180	1.319	1.714	2.069	2.500	2.807	3.485
24	0.256	0.436	0.685	0.857	1.179	1.318	1.711	2.064	2.492	2.797	3.467
25	0.256	0.436	0.684	0.856	1.178	1.316	1.708	2.060	2.485	2.787	3.450
26	0.256	0.436	0.684	0.856	1.177	1.315	1.706	2.056	2.479	2.779	3.435
27	0.256	0.435	0.684	0.855	1.176	1.314	1.703	2.052	2.473	2.771	3.421
28	0.256	0.435	0.683	0.855	1.175	1.313	1.701	2.048	2.467	2.763	3.408
29	0.256	0.435	0.683	0.854	1.174	1.311	1.699	2.045	2.462	2.756	3.396
30	0.256	0.435	0.683	0.854	1.173	1.310	1.697	2.042	2.457	2.750	3.385
35	0.255	0.434	0.682	0.852	1.170	1.306	1.690	2.030	2.438	2.724	3.340
40	0.255	0.434	0.681	0.851	1.167	1.303	1.684	2.021	2.423	2.704	3.307
45	0.255	0.434	0.680	0.850	1.165	1.301	1.679	2.014	2.412	2.690	3.281
50	0.255	0.433	0.679	0.849	1.164	1.299	1.676	2.009	2.403	2.678	3.261
55	0.255	0.433	0.679	0.848	1.163	1.297	1.673	2.004	2.396	2.668	3.245
60	0.254	0.433	0.679	0.848	1.162	1.296	1.671	2.000	2.390	2.660	3.232
∞	0.253	0.431	0.674	0.842	1.150	1.282	1.645	1.960	2.326	2.576	3.090