Data provided: Formula Sheet, incorporating Critical Values Tables

**MAS361**

The University Of Sheffield.

**SCHOOL OF MATHEMATICS AND STATISTICS** **Autumn Semester 2015–16**

**Medical Statistics** **2 hours**

*Candidates may bring to the examination a calculator that conforms to University regulations. All questions will be marked, but credit will be given for only the best* ***THREE*** *answers. All questions carry equal marks. Total marks 60.*

**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** Withdrawals can cause problems in clinical trials.

(i) Using a 'Worst Case Scenario' (WCS) approach to attribution of unknown outcomes where appropriate, provide both

(a) per protocol *(4 marks)*

and

(b) intention to treat *(4 marks)*

analyses of the following (artificial) data from a trial comparing Drug with Placebo?

| Assessment | Drug | Placebo | TOTAL |
|---:|---:|---:|---:|
| Success | 20 | 20 | 40 |
| Failure | 4 | 16 | 20 |
| Total Assessed | 24 | 36 | 60 |
| Withdrawn | 16 | 4 | 20 |
| Total Randomized | 40 | 40 | 80 |

(c) Explain why the WCS approach is not easy when the primary end-point is quantitative. *(2 marks)*

(d) Which analysis do you feel is more appropriate and why? *(2 marks)*

(e) What is your overall conclusion about the value of the Drug? *(2 marks)*

(ii) If the trial coordinator adopted conventional values for many of the parameters in his sample size calculations, namely

20% allowance for dropouts
5% probability of a type I error
90% power

and the success rate on Placebo was only anticipated to be 50%, what Clinically Relevant Difference was the trial sized to detect? *(6 marks)*

**2** A randomized, double-blind comparative trial of drugs A and B is to be conducted. A statistician proposes that the small (16 patient) study might be conducted according to the following schematic diagram

| Drug A before after | Drug B before after |
|:---:|:---:|
| $X \longleftrightarrow X$ | $X \longleftrightarrow X$ |
| $X \longleftrightarrow X$ | $X \longleftrightarrow X$ |
| $\vdots$ | $\vdots$ |
| $X \longleftrightarrow X$ | $X \longleftrightarrow X$ |

where '$X$' indicates that the quantitative response is measured and measurements on the same patient are linked. Thus measurments are taken both before and after application of the drug.

 Question 2 continued on next page

**2** (continued)

The following summary statistics for the original responses (A before, A after, B before, B after), and some derived variables, are available:

| | $n$ | mean | s.d. |
|---|---|---|---|
| A before | 8 | 96.1 | 17.53 |
| A after | 8 | 92.4 | 17.14 |
| B before | 8 | 89.5 | 17.63 |
| B after | 8 | 91.1 | 17.26 |
| A after - A before | 8 | −3.8 | 2.19 |
| B after - B before | 8 | 1.6 | 4.34 |
| B before - A before | 8 | −6.6 | 5.45 |
| B after - A after | 8 | −1.3 | 5.01 |

(i) Suggest how you might test whether or not the drugs had the same effect using the summary statistics available. ***(4 marks)***

(ii) State the distributional assumptions underpinning your suggestion in part (i). ***(2 marks)***

(iii) Assuming the assumptions are valid, use appropriate values from the summary statistics given to perform the test you suggested in (i). ***(3 marks)***

(iv) Explain why such a study might be preferable to the simpler trial (of the same size) represented in the following schematic diagram. ***(2 marks)***

| Drug A | Drug B |
|---|---|
| $X$ | $X$ |
| $X$ | $X$ |
| $\vdots$ | $\vdots$ |
| $X$ | $X$ |

(v) The 16 patients are required to be allocated randomly to the two groups. Explain the benefits of a blocked allocation over a simple random allocation. ***(2 marks)***

(vi) Suppose the effects of the drugs are thought to depend on the sex (Male/Female) and smoking status (Non-smoker/Smoker) of the patients.

(a) Explain how this would affect the analysis you would advise for the trial. ***(2 marks)***

(b) Explain how this would affect the randomization you would advise. ***(1 mark)***

**2** (continued)

(c) If the sex and smoking status of the patients are as given below, use the following random digits
3 0 4 5 8 4 9 2 0 7 6 2 3 5 8 4 1 5 3 2 . . . .
to allocate the 16 patients to the two drugs. Explain your procedure clearly. ***(4 marks)***

| Patient number | Sex | Smoking status |
|---|---|---|
| 1 | Male | Smoker |
| 2 | Male | Smoker |
| 3 | Female | Smoker |
| 4 | Male | Non-smoker |
| 5 | Male | Smoker |
| 6 | Male | Non-smoker |
| 7 | Male | Smoker |
| 8 | Female | Non-smoker |
| 9 | Male | Non-smoker |
| 10 | Female | Non-smoker |
| 11 | Male | Smoker |
| 12 | Female | Non-smoker |
| 13 | Male | Non-smoker |
| 14 | Male | Non-smoker |
| 15 | Male | Smoker |
| 16 | Male | Smoker |

**3** 24 patients with multiple myeloma (a type of cancer arising from plasma cells) were allocated to one of two forms of treatment and followed up. 11 patients were given drug $A$ and 13 patients drug $B$. The primary outcome of interest was mortality. The table below shows the data collected. Here the status variable records whether the patient was observed to die (status = 1) or whether they were lost to follow-up beforehand (status = 0).

 Question 3 continued on next page

| | Drug A | | Drug B | |
|---|---|---|---|---|
| | Time (mths) | Status | Time (mths) | Status |
| | 18.70 | 1 | 8.90 | 0 |
| | 1.40 | 1 | 14.90 | 1 |
| | 0.40 | 1 | 14.80 | 0 |
| | 9.20 | 1 | 16.50 | 0 |
| | 12.40 | 1 | 14.10 | 1 |
| | 23.70 | 1 | 13.80 | 1 |
| | 12.10 | 1 | 12.80 | 1 |
| | 3.10 | 0 | 11.10 | 0 |
| | 26.40 | 0 | 19.50 | 1 |
| | 33.50 | 0 | 17.30 | 0 |
| | 6.50 | 1 | 9.30 | 1 |
| | | | 19.90 | 1 |
| | | | 10.50 | 1 |
| Total | 147.4 | 8 | 183.4 | 8 |

**3** (continued)

Some R analysis is shown below:

```
> t1 <- c(18.7,1.4,0.4,9.2,12.4,23.7,12.1,3.1,26.4,33.5,6.5)
> t2 <- c(8.9,14.9,14.8,16.5,14.1,13.8,12.8,11.1,19.5,17.3,9.3,19.9,10.5)
> time <- c(t1, t2)
>
> c1 <- c(1,1,1,1,1,1,1,0,0,0,1)
> c2 <- c(0,1,0,0,1,1,1,0,1,0,1,1,1)
> status <- c(c1, c2)
>
> type <- rep(c("A", "B"), c(11, 13))
>
> Comp.sv <- Surv(time, status, type = "right")
```

 Question 3 continued on next page

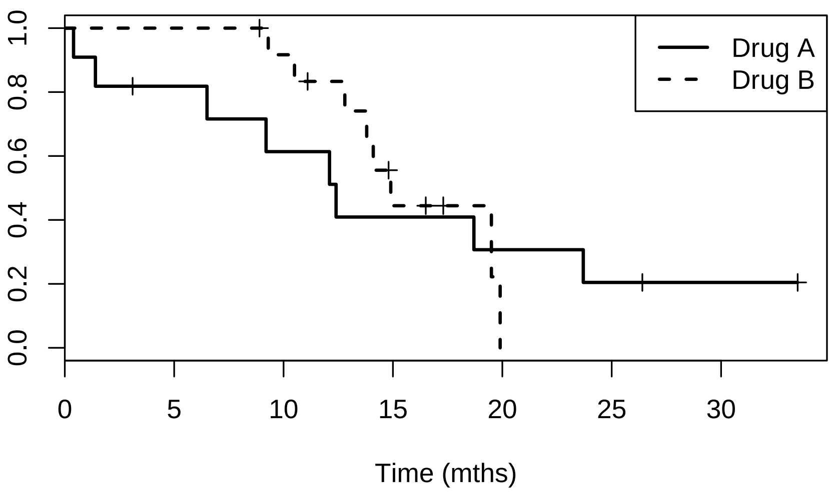
**3** (continued)

```
> summary(survfit(Comp.sv ~ type))
Call: survfit(formula = Comp.sv ~ type)

                type=A
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
  0.4     11       1    0.909  0.0867       0.7541        1.000
  1.4     10       1    0.818  0.1163       0.6192        1.000
  6.5      8       1    0.716  0.1397       0.4884        1.000
  9.2      7       1    0.614  0.1526       0.3769        0.999
 12.1      6       1    0.511  0.1578       0.2793        0.936
 12.4      5       1    0.409  0.1559       0.1939        0.863
 18.7      4       1    0.307  0.1467       0.1202        0.783
 23.7      3       1    0.205  0.1286       0.0597        0.701

                type=B
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
  9.3     12       1    0.917  0.0798       0.7729        1.000
 10.5     11       1    0.833  0.1076       0.6470        1.000
 12.8      9       1    0.741  0.1295       0.5259        1.000
 13.8      8       1    0.648  0.1426       0.4211        0.998
 14.1      7       1    0.556  0.1493       0.3281        0.941
 14.9      5       1    0.444  0.1554       0.2240        0.882
 19.5      2       1    0.222  0.1753       0.0474        1.000
 19.9      1       1    0.000     NaN           NA           NA

> plot(survfit(Comp.sv ~ type), lty = c(1,2), lwd = 2, xlab = "Time (mths)")
```




(i) Without making any model assumptions, estimate the median mortality times for the two drugs. *(3 marks)*

**3** (continued)

(ii) It is suggested that the survival times are Exponentially distributed with rates $\lambda_A$ and $\lambda_B$ respectively. Under this assumptions:

(a) Estimate $\lambda_A$ and $\lambda_B$ and hence the mean mortality times with approximate 95% confidence intervals. ***(4 marks)***

(b) Perform a likelihood ratio test to assess whether there is a difference in the mortality time distributions of the two drugs. ***(4 marks)***

(iii) Use the partially complete R output (the `???`s indicate output which is missing)

```
> survdiff(Comp.sv ~ as.factor(type))
Call:
survdiff(formula = Comp.sv ~ as.factor(type))

                    N Observed Expected   ???
as.factor(type)=A 11        8     7.55   ???
as.factor(type)=B 13        8     8.45   ???
```

to perform a non-parametric test assessing whether there is a difference in mortality between the two drugs. ***(3 marks)***

(iv) Do the assumptions of an Exponential survival distribution seem plausible? Explain your answer. ***(2 marks)***

(v) Discuss the impact on your analysis if:

(a) patients were withdrawn from the study if their condition was seen to be deteriorating or they showed side effects which needed alternative treatment. ***(2 marks)***

(b) patients withdrew from the study because they were feeling better and no longer needed continuing treatment. ***(2 marks)***

**4** A clinical trial was conducted to compare two treatments for breast cancer among women. After removal of the tumour, patients were randomly allocated to either treatment A or treatment B and followed up for 5 years for cancer recurrence. The data are stored in `breast` and coding for the different variables is shown below:

Coding:
Treat: treatment (0 = treatment A; 1 = treatment B)
Obese: indicator if patient is obese (0 = non-obese; 1 = obese)
Age: age of patient centred on 50 years (i.e. 55 year old is +5)
Time: time until cancer recurrence (years)
Status: indicator of relapse (1) or censoring (0)

 Question 4 continued on next page

**4** (continued)

(i) Some R analysis was performed with the edited output shown below:

```
> Breast.sv <- Surv(Time, Status)
>
> Br.fit <- coxph(Breast.sv ~Obese+Treat+Age)
> summary(Br.fit)
Call:
coxph(formula = Breast.sv ~ Obese + Treat + Age)

  n= 200, number of events= 170

           coef exp(coef)  se(coef)      z Pr(>|z|)
Obese  0.221694  1.248189  0.155460  1.426 0.153855
Treat -0.537459  0.584231  0.158781 -3.385 0.000712 ***
Age    0.023620  1.023902  0.007944  2.973 0.002945 **
---
```

(a) Specify the form of the model used for the above analysis in terms of the baseline hazard function $h_0(t)$ and the covariates. ***(3 marks)***

(b) Describe in detail the effects of the covariates on the time to recurrence. ***(4 marks)***

(c) Using the model output, calculate the estimate of the hazard ratio comparing

- An *obese* 56 year old woman on treatment A
- A *non-obese* 43 year old woman on treatment B

***(3 marks)***

(ii) An alternative analysis is shown below

```
> Br.fit1 <- survreg(Breast.sv ~Obese+Treat+Age, dist="exponential")
> summary(Br.fit1)

Call:
survreg(formula = Breast.sv ~ Obese + Treat + Age, dist = "exponential")
              Value Std. Error     z        p
(Intercept)  0.6274    0.14495  4.33 0.000015
Obese       -0.2094    0.15447 -1.36 0.175219
Treat        0.5825    0.15563  3.74 0.000182
Age         -0.0251    0.00769 -3.27 0.001085

Scale fixed at 1

Exponential distribution
Loglik(model)= -266.1   Loglik(intercept only)= -281
Chisq= 29.91 on 3 degrees of freedom, p= 1.4e-06
Number of Newton-Raphson Iterations: 5
n= 200
```

 Question 4 continued on next page

**4** (continued)

(a) Specify what type of analysis has been performed here and write down the fitted model for $T$, the time to recurrence. ***(4 marks)***

(b) Comment on the effects of the different covariates on the time to recurrence with this approach. Would you prefer to be on treatment A or B? ***(3 marks)***

(c) Estimate the expected time to recurrence for a 56 year old obese woman who is taking treatment B. ***(3 marks)***

## End of Question Paper

# STANDARD FORMULAE FOR MEDICAL STATISTICS (INCLUDING TABLES OF CRTICAL 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** $r = n_1 + n_2 - 2$

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

**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 $\lambda$ with censoring** The mle

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

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

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

so e.g.

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

**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**

$$2\left\{\Delta_1 \log \frac{\Delta_1}{\mathcal{T}_1} + \Delta_2 \log \frac{\Delta_2}{\mathcal{T}_2} - (\Delta_1 + \Delta_2) \log \frac{\Delta_1 + \Delta_2}{\mathcal{T}_1 + \mathcal{T}_2}\right\} \approx \chi_1^2$$

**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 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 $\nu$). 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 $\Phi^{-1}$ 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(`$p$, $\nu$`)` where $p$ is percentage, e.g. for 95%, $p = 0.95$

| $\nu$ | 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%, $p = 0.95$

| $\nu$ | 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 |
| $\infty$ | 0.253 | 0.431 | 0.674 | 0.842 | 1.150 | 1.282 | 1.645 | 1.960 | 2.326 | 2.576 | 3.090 |