# MATH 1323

## SOLUTIONS For HW#9

I. [#3, #4, #5 on p.34 of SPS]

$\boxed{\#3}$ Using Tables 8-F and 8-G on pp 30-31 of the first Health Canada group, the May 14 results give us two samples each of size $n=8$

| Test Group | | Reference Group | |
|---|---|---|---|
| Subject | Test $AUC_T$ | Subject | Reference $AUC_T$ |
| A | 365 | B | 595 |
| E | 233 | C | 471 |
| G | 178 | F | 257 |
| I | 408 | H | 382 |
| L | 140 | K | 218 |
| M | 165 | N | 106 |
| P | 122 | O | 290 |
| R | 275 | Q | 144 |

We put the 8 Test $AUC_T$ values in list $L_1$ and the 8 Reference $AUC_T$ values in list $L_2$

With $\mu_1$ and $\mu_2$ the mean values of the random variables Test $AUC_T$ and Reference $AUC_T$ the null hypothesis $H_0: \mu_1 = \mu_2$ vs the alternative hypothesis $H_1: \mu_1 \neq \mu_2$ is tested using 2 Samp T Test $\boxed{\text{DATA}}$ and entering the lists $L_1$ and $L_2$ with $\mu_1: \boxed{\neq} \mu_2$ and Pooled: $\boxed{\text{Yes}}$ to obtain $t =$ ~~-1.039~~ $-1.036$

p-value $= .318$

Since the p-value is $> .10$, we $\boxed{\text{accept } H_0}$ at $\alpha = .10$ [or at any $\alpha$ up to .318]

$\boxed{\#4}$ We obtain a 90% confidence interval for $\mu_1 - \mu_2$ using 2-Samp T Int $\boxed{\text{Data}}$ and entering the lists $L_1$ and $L_2$ along with C-Level : .90 and Pooled : $\boxed{\text{Yes}}$. The result is the interval (−194.8 [redacted], 50.5 [redacted])

Since 0 is in this interval, we confirm the result of $\boxed{\#3}$, i.e. Ho is accepted at the level $\alpha = .10$

$\boxed{\#5}$ The length of the confidence interval in #4 is 50.5 [redacted] − (−194.8) = [redacted] 245.3

In contrast, the solution to $\boxed{\#2}$ provided the 90% confidence interval (−67.81, 23.06) for $\mu_1 - \mu_2$ using the paired test and reference $AUC_T$ data for the 16 subjects. The length of this interval is $23.06 - (-67.81) = 90.9$.

The ratio of these lengths is $\frac{245.3}{90.9}$ = [redacted] 2.70

<u>Conclusions</u>: Dropping the paired comparison of test and reference $AUC_T$ for each subject and using only the May 14 data with 2 separate samples was a <u>terrible</u> procedure. It gave a confidence interval nearly [redacted] 3 times as big with virtually no chance to argue that the data provide evidence supporting $\mu_1 \neq \mu_2$. In general, paired comparison tests are much more powerful (more apt to allow Ho to be rejected) than non-paired 2 sample tests.

II. Using the data in Tables 8-G and 8-J we wish to compute 90% confidence intervals for the geometric means of the random variables Relative $AUC_T$ and Relative $C_{max}$

Procedure: (1) Let $L_1 = \{97, 68, 149, \ldots, 47, 80\}$ and $L_2 = \{97, 49, 164, \ldots, 31, 61\}$ be the lists of Relative $AUC_T$ and Relative $C_{max}$ dat[a]

(2) Let $L_3 = \ln(L_1)$, $L_4 = \ln(L_2)$

(3) Using T-Interval $\boxed{\text{Data}}$ first with list $L_3$ and next with list $L_4$ and with C-Level : .90 yields the intervals $(4.3093, 4.6378)$ and $(4.1192, 4.6643)$

Conclusion: Since neither interval is contained in (80%, 125%) the test drug fails the bioequivalence test.

(4) The desired 90% confidence intervals for the geometric means are

$$\left(e^{4.3093}, e^{4.6378}\right) = (74.4\%, 103.3\%)$$

and

$$\left(e^{4.1192}, e^{4.6643}\right) = (61.5\%, 106.1\%)$$

These are in very close agreement with the intervals (74%, 104%) and (61%, 107%) computed in Tables 8-I and 8-L by Health Canada with a more elaborate method.

Variations: (a) Enter instead the decimals $L_1 = \{.97, .68, \ldots, .80\}$ and $L_2 = \{.97, .49, \ldots, .61\}$ and proceed as in Steps 2-4 to get the same results

(b) Enter the difference in ln values from Tables 8-G and 8-J. Again the results are the same.

III. [#22, #26, #36 on pp. 571-2, § 8.1]

$\boxed{\#22}$ $a_n = \dfrac{\ln(2+e^n)}{3n}$

Method 1: $a_n = f(n)$ for $f(x) = \dfrac{\ln(2+e^x)}{3x}$. By l'Hôpital's Rule,

$$\lim_{x\to\infty} f(x) = \lim_{x\to\infty} \frac{\frac{d}{dx}\{\ln(2+e^x)\}}{\frac{d}{dx}(3x)}$$

$$= \lim_{x\to\infty} \frac{e^x}{3(2+e^x)}$$

$$= \lim_{x\to\infty} \frac{1}{3}\left(\frac{1}{2e^{-x}+1}\right)$$

$$= 1/3$$

so $\boxed{\lim_{n\to\infty} a_n = 1/3}$, i.e. $\{a_n\}_{n\geq 1}$ converges to $1/3$

Method 2: $\ln(2+e^n) = \ln(e^n(2e^{-n}+1)) = \underbrace{\ln(e^n)}_{n} + \ln(2e^{-n}$

and $2e^{-n}+1 \to 1$ as $n \to \infty$

So $a_n = \dfrac{n + \ln(2e^{-n}+1)}{3n} = \dfrac{1}{3} + \dfrac{1}{3n}\ln(2e^{-n}+1)$

$\longrightarrow 1/3$ as $n \to \infty$

i.e. $\boxed{\lim_{n\to\infty} a_n = 1/3}$

$\boxed{\#26}$ $a_n = \dfrac{(-3)^n}{n!} = (-1)^n \dfrac{3}{n}\dfrac{3}{n-1}\cdots\dfrac{3}{4}\left(\dfrac{3\cdot 3\cdot 3}{3\cdot 2\cdot 1}\right)$

For $n \geq 4$, there are $n-3$ factors of the form $\frac{3}{k}$ with $k \geq 4$ [redacted] and each is $\leq 3/4$ so

$|a_n| \leq (3/4)^{n-3}\ 9/2$

Since $(3/4)^{n-3} \longrightarrow 0$ as $n \to \infty$

$\lim_{n\to\infty} |a_n| = 0$ and this implies

$\boxed{\lim_{n\to\infty} a_n = 0}$

$\boxed{\#36}$ (a) In general, if $\lim_{n\to\infty} a_n = L$ then $a_n \to L$ as $n \to \infty$ so

$a_{n+1}$ also $\to L$ as $n \to \infty$, i.e. $\lim_{n\to\infty} a_{n+1} = L$

(b) Let $a_1 = 1$ and $a_{n+1} = \frac{1}{1+a_n}$.

| $n$ | Fraction Expression for $a_n$ | Decimal Expression for $a_n$ |
|---|---|---|
| 1 | $1$ | 1.00000 |
| 2 | $\frac{1}{1+1} = \frac{1}{2}$ | .50000 |
| 3 | $\frac{1}{1+1/2} = 2/3$ | $.\overline{666}$ |
| 4 | $\frac{1}{1+2/3} = 3/5$ | .60000 |
| 5 | $\frac{1}{1+3/5} = 5/8$ | .62500 |
| 6 | $\frac{1}{1+5/8} = 8/13$ | .61538 |
| 7 | $\frac{1}{1+8/13} = 13/21$ | .61905 |
| 8 | $\frac{1}{1+13/21} = 21/34$ | .61764 |
| 9 | $\frac{1}{1+21/34} = \frac{34}{55}$ | .61818 |
| 10 | $\frac{1}{1+\frac{34}{55}} = \frac{55}{89}$ | .61798 |

This leads us to conjecture that $\lim_{n\to\infty} a_n = L$ exists and that $L = .618$ to 3 decimal places

(c) Suppose $L = \lim_{n\to\infty} a_n$ exists. By (a)

$$L = \lim_{n\to\infty} a_{n+1} = \lim_{n\to\infty}\left[\frac{1}{1+a_n}\right] = \frac{1}{1+\lim_{n\to\infty} a_n} = \frac{1}{1+L}$$

so $L + L^2 = 1$ with $L > 0$. By the quadratic formula

$$L = -\tfrac{1}{2} + \tfrac{1}{2}\sqrt{5} = .618033988 7\ldots$$

Remark: Each $a_n$ is the ratio of two successive terms in the Fibonacci series $1, 1, 2, 3, 5, 8, 13, 21, 34, 55, 89, \ldots$ One can show that the $n^{th}$ term in the Fibonacci series is $\left(\frac{3-\sqrt{5}}{2}\right)\left(\frac{\sqrt{5}+1}{2}\right)^{n-1} + \left(\frac{\sqrt{5}-1}{2}\right)^{n}$ and use this to prove $\lim_{n\to\infty} a_n$ exists.