

“BIVARIATE DISTRIBUTION” FOR INFRASTRUCTURES AMONG OPERATIVE, NATURAL AND NO MENOPAUSES

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Received 2014-08-15; Revised 2014-08-19; Accepted 2014-08-22

ABSTRACT

Menopause is not an illness but rather an important event as it changes the body physiology and mental cognition via hormonal changes. During data analysis of menopause incidence data, new *bivariate distribution* is discovered. Their *marginal, conditional distribution and statistical properties* including the inter and partial correlations are explored and utilized to interpret menopause data. A likelihood ratio hypothesis testing procedure is constructed to test the statistical significance of the sample estimate of the *chance for menopause* and estimate of the *chance for operative menopause*. The menopause data are analyzed and interpreted in the illustration. Research directions for future work are pointed out.

Keywords: Likelihood Ratio Test, Multinomial Count Distribution, Hypothesis Testing, P-Value, Statistical Power

1. INTRODUCTION

The Menopause is the cessation of a woman's reproductive ability, the opposite of menarche. Menopause is the permanent cessation of menstruation resulting from loss of ovarian follicular activity. Medically speaking, the date of menopause is the day after the final episode of menstrual flow finishes. Menopause occurs in species of nonhuman primates also. *Perimenopause* is a term for the menopause transition years, the time both before and after the last period ever, while hormone levels are still fluctuating erratically. The average age of menopause is 51. During peri-and post menopause period, changes occur in hormonal patterns, which induce menopausal symptoms. Recently, Al-Jawadi (2014) reported that the hormones T3 and T4 are biomarkers of uterine cancer especially after the menopause.

Menopause is not a disease that has to be treated. The woman needs help if symptoms like hot flashes appear. Hot flashes and mood changes are common symptoms of perimenopause. Other symptoms are *palpitations, psychological effects such as depression, anxiety, irritability, memory problems and lack of concentration and*

atrophic effects such as vaginal dryness and urgency of urination. Other side effects of the menopausal transition are *lack of sexual desire or libido, lack of sexual arousal and vaginal dryness*. Changing levels of estrogen and progesterone, which are two female hormones made in your ovaries, might lead to symptoms. Menopause is linked to illness cancer (Tavani *et al.*, 2000; Paganini-Hill *et al.*, 1984), heart disease (Paganini-Hill *et al.*, 1984; Hu *et al.*, 1999; Joakimsen *et al.*, 2000; Jacobsen *et al.*, 1999), osteoporosis and bone loss (Van Der Schouw *et al.*, 1996; Ohta *et al.*, 1996; Cheng *et al.*, 1997; Osei-Hyiaman *et al.*, 1998; Hadjidakis *et al.*, 1999; Luisetto *et al.*, 1995) and depression (Harlow and Signorello, 2000) and overall mortality (Treloar, 1981).

Age of menopause is a significant factor. The time between the onset of perimenopause and the final menstrual period is about 4 years (Crawford, 2000; Main *et al.*, 2013; Orleans *et al.*, 2014). The *operated menopause* is surgically done with hormone replacement therapy in a medical treatment. In operative menopause, instead of declining slowly the levels of estrogens and testosterone over time, they decline sharply, resulting in more severe symptoms.

During an analysis of menopause data, new *bivariate distribution* is discovered and they are named *bivariate menopause distribution* in this article. The marginal, conditional and statistical properties of the *menopause distribution* is constructed. Expressions for the inter, partial and semi-partial correlations among the operative, natural and no menopauses are derived. The likelihood ratio hypothesis testing procedures are constructed and illustrated using the menopause data in Macmahon and Worcester (1966). Research directions for future work on *bivariate menopause distribution* is discussed.

2. BIVARIATE MENOPAUSE DISTRIBUTION AND ITS PROPERTIES

To be specific, let $0 < \phi < 1$ be an unknown chance for a woman in a known age to have a menopause. Among those who have the menopause, it might have happened in one of two mutually exclusive ways. They are *operative and natural menopause*. Let $0 < \theta < 1$ be an unknown *conditional chance* for the menopause is due to an *operative* medical procedure. Implicitly, the unknown *conditional chance* for a woman with menopause due to natural cause is $1-\theta$. Their interconnections are displayed schematically in a Venn diagram (Fig. 1).

The upper portion within the circle in the square denotes an unknown chance $\phi(1-\theta)$ for a woman to have a *natural menopause*. The lower portion in the circle represents the unknown chance $\phi\theta$ for a woman to have an *operative menopause*. The segment outside the circle but within the square denotes the unknown chance $1-\phi$ for a woman to have *no menopause*. In other words, the lower pie ABO has an area $\phi\theta$ while the upper pie has an area $\phi(1-\theta)$.

Suppose a random sample of n women is drawn in a study and they are classified into the number x of operative menopause cases, the number y of natural menopause cases and the number $z = n-x-y$ of no menopause cases. Their Probability Mass Function (PMF) is:

$$\begin{aligned} \Pr(x, y | \phi, \theta, n) &= \frac{n!}{x!y!(n-x-y)!} (1-\phi)^n \\ &\left(\frac{\phi}{1-\phi}\right)^{x+y} \theta^x (1-\theta)^y; \\ x, y &= 0, 1, 2, \dots, n; 0 < \phi, \theta < 1. \end{aligned} \tag{1}$$

It is straightforward exercise to check that

$$\Pr(x, y | \phi, \theta, n) \geq 0 \text{ and } \sum_{x=0}^n \sum_{y=0}^n \Pr(x, y | \phi, \theta, n) = 1.$$

The *pmf* (1) is named “*bivariate menopause distribution*” since it is new to the literature. The marginal *pmf* of the number of operative menopause cases is:

$$\begin{aligned} \Pr(x | \phi, \theta, n) &= \sum_{y=0}^n \Pr(x, y | \phi, \theta, n) \\ &= \frac{n!}{x!(n-x)!} (1-\phi\theta)^n \left(\frac{\phi\theta}{1-\phi\theta}\right)^x; \\ x &= 0, 1, 2, \dots, n; 0 < \phi, \theta < 1. \end{aligned} \tag{2}$$

The *pmf* (2) is named “*operative menopause distribution*”. The conditional *pmf* of the number of natural menopause for given number of operative menopause cases is:

$$\begin{aligned} \Pr(y | x, \phi, \theta, n) &= \frac{\binom{n-x}{y} \left(\frac{\phi(1-\theta)}{1-\phi}\right)^y}{\left(\frac{1-\phi\theta}{1-\phi}\right)^{n-x}}; \\ y &= 0, 1, 2, \dots, n-x; 0 < \phi, \theta < 1. \end{aligned} \tag{3}$$

Comparing (3) with the marginal *pmf* of the number of natural menopause cases is:

$$\begin{aligned} \Pr(y | \phi, \theta, n) &= \sum_{x=0}^n \Pr(x, y | \phi, \theta, n) \\ &= \frac{n!}{y!(n-y)!} \left(\frac{\phi[1-\theta]}{1-\phi[1-\theta]}\right)^y (1-\phi[1-\theta])^n; \\ y &= 0, 1, 2, \dots, n; 0 < \phi, \theta < 1, \end{aligned} \tag{4}$$

It is clear that the random variables x and y are *not independent*. The random variables are correlated and we will obtain their correlation coefficient later. The *pmf* (4) is named “*natural menopause distribution*”. The conditional *pmf* of the number of operative menopauses for given number of natural menopause cases is:

$$\begin{aligned} \Pr(x | y, \phi, \theta, n) &= \binom{n-y}{x} \left(\frac{\phi\theta}{1-\phi}\right)^x / \left(\frac{1-\phi[1-\theta]}{1-\phi}\right)^{n-y}; \\ x &= 0, 1, 2, \dots, n-y; 0 < \phi, \theta < 1 \end{aligned} \tag{5}$$

A comparison of (5) with (2) confirms that the random variables x and y are *not independent*. How much are they correlated? For this purpose, we find their means:

$$\mu_x = \sum_{x=0}^n x \Pr(x | \phi, \theta, n) = n\phi\theta$$

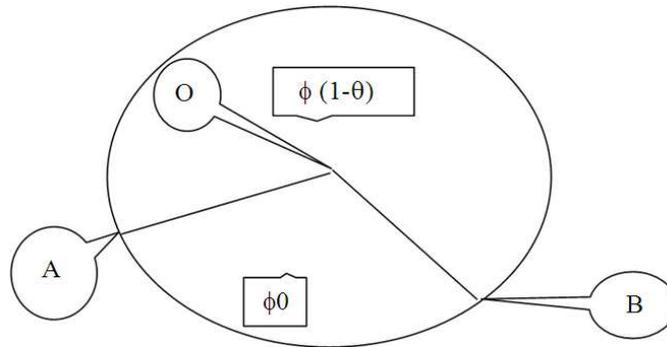


Fig. 1. Venn diagram of menopause and causes

And:

$$\mu_y = \sum_{x=0}^n y \Pr(y|\phi, \theta, n) = n\phi(1-\theta)$$

Their variances are:

$$\sigma_x^2 = \sum_{x=0}^n (x - \mu_x)^2 \Pr(x|\phi, \theta, n) = n\phi\theta(1-\phi\theta) \tag{6}$$

$$\sigma_y^2 = \sum_{x=0}^n (y - \mu_y)^2 \Pr(y|\phi, \theta, n) = n\phi(1-\theta)(1-\phi[1-\theta]) \tag{7}$$

And:

$$\begin{aligned} \sigma_{x,y} &= \text{cov}(x, y) \\ &= \sum_{x=0}^n \sum_{y=0}^n (x - \mu_x)(y - \mu_y) \Pr(x, y|\phi, \theta, n) \\ &= \frac{n\phi^2\theta(1-\theta)}{(1-\phi)} [n\phi - 1 - (n-1)\phi\theta] \end{aligned} \tag{8}$$

Hence, the correlation between the number, x of the operative menopause and the number, y of the natural menopause is:

$$\begin{aligned} \rho_{x,y} &= \text{corr}(x, y) \\ &\approx n\phi(1-\theta) \left(\frac{\phi}{1-\phi} \right) \sqrt{\frac{\theta(1-\theta)}{[(1-\phi) + \phi^2\theta(1-\theta)]}} \end{aligned} \tag{9}$$

It is quite natural for anyone to ask: How are the number, x of the operative menopause and the number, z of the no menopause is correlated in comparison to how are the number, y of the natural menopause and the number, z of the no menopause is correlated? These questions are answerable as follows. For this purpose, note that:

$$\begin{aligned} \mu_z &= E(Z|\phi, \theta, n) = \\ E(n - X - Y|\phi, \theta, n) &= (n - \mu_x - \mu_y) \end{aligned} \tag{10}$$

And:

$$\sigma_z^2 = \text{var}(Z|\phi, \theta, n) = \sigma_x^2 + \sigma_y^2 - 2\sigma_{x,y} \tag{11}$$

The covariance between x and z is $\sigma_{x,z} = \text{cov}(X, Z) = -(\sigma_x^2 + \sigma_{x,y})$. Hence, the correlation level between the number, x of the operative menopause and the number, z of the no menopause is:

$$\rho_{x,z} = \text{corr}(X, Z) = - \frac{\left(\frac{\sigma_x}{\sigma_y} + \rho_{x,y} \right)}{\sqrt{\left(1 + \frac{\sigma_x^2}{\sigma_y^2} - 2 \frac{\sigma_x}{\sigma_y} \rho_{x,y} \right)}} \tag{12}$$

where, $\rho_{x,y}$, σ_x^2 and σ_y^2 are specified in (12), (6) and (7) respectively. It is interesting to witness that the correlation (12) does not diminish to zero but rather to

$\rho_{x,z} \rightarrow - \frac{\sigma_x}{\sqrt{(\sigma_y^2 + \sigma_x^2)}}$ even the correlation (9) weakens to zero (that is, $\rho_{x,y} \rightarrow 0$).

Proceeding likewise, we obtain that the covariance between y and z is $\sigma_{y,z} = \text{cov}(Y, Z) = -(\sigma_y^2 + \sigma_{x,y})$. Hence, the correlation level between the number, y of the natural menopause and the number, z of the no menopause is:

$$\rho_{y,z} = \text{corr}(Y, Z) = - \frac{\left(\frac{\sigma_y}{\sigma_x} + \rho_{x,y} \right)}{\sqrt{\left(1 + \frac{\sigma_y^2}{\sigma_x^2} - 2 \frac{\sigma_y}{\sigma_x} \rho_{x,y} \right)}} \tag{13}$$

It is interesting to notice that the correlation (13) does not diminish to zero but rather to $\rho_{y,z} \rightarrow -\frac{\sigma_y}{\sqrt{(\sigma_y^2 + \sigma_x^2)}}$ even the correlation (9) weakens to zero (that is, $\rho_{x,y} \rightarrow 0$).

Incidentally, it means that even when the number, x of the operative menopauses and the number, y of the natural menopauses weakens to zero, they are glued together with a circular relationship $\rho_{x,z}^2 + \rho_{y,z}^2 = 1$ with a radius one (Fig. 2).

What happens when the correlations between the number, x of the operative menopauses or the number, z of the no menopauses (that is, $\rho_{x,z} \neq 0$) and between the number, y of the operative menopauses and the number, z of the no menopauses (that is, $\rho_{y,z} \neq 0$) are non-negligible? After an adjustment based on the number, z no menopauses, the *partial correlation*, $\rho_{(x,y)|z}$ between the number, x of the operative menopauses and the number, y of the natural menopauses is:

$$\rho_{(x,y)|z} = \frac{\rho_{x,y} - \rho_{x,z}\rho_{y,z}}{\sqrt{(1 - \rho_{x,z}^2)(1 - \rho_{y,z}^2)}} \tag{14}$$

Suppose that a change in the number, z of no menopauses impacts only the number, x of the operated menopauses but not the number, y of the natural menopauses, the adjusted (for z) correlation between the number, x of operated menopauses and the number, y of the natural menopauses is *semi-partial correlation*, $s\rho_{(x,y)|z \rightarrow x}$ and it is:

$$s\rho_{(x,y)|z \rightarrow x} = \frac{\rho_{x,y} - \rho_{x,z}\rho_{y,z}}{\sqrt{1 - \rho_{x,z}^2}} \tag{15}$$

On the contrary, if a change in the number, z of no menopauses impacts only the number, y of the natural menopauses but not the number, x of the operated menopauses, the adjusted (for z) correlation between the number, x of operated menopauses and the number, y of the natural menopauses is *semi-partial correlation*, $s\rho_{(x,y)|z \rightarrow y}$ and it is:

$$s\rho_{(x,y)|z \rightarrow y} = \frac{\rho_{x,y} - \rho_{x,z}\rho_{y,z}}{\sqrt{1 - \rho_{y,z}^2}} \tag{16}$$

One wonders how much is an *index of increase*, $i_{(x,y)|z \rightarrow (x,y)}$ in the relationship between the number, x of

operated menopauses and the number, y of the natural menopauses when the number, z no menopauses impacts the number, y of the natural menopauses in addition to the number, x of operated menopauses. This is captured using (14) and (15). That is:

$$i_{(x,y)|z \rightarrow (x,y)} = \left\{ \frac{\rho_{(x,y)|z}}{s\rho_{(x,y)|z \rightarrow x}} \right\} = \frac{1}{1 + \sqrt{1 - \rho_{y,z}^2}} \tag{17}$$

Similarly, an *index of increase*, $i_{(x,y)|z \rightarrow (x,y)}$ in the relationship between the number, x of operated menopauses and the number, y of the natural menopauses is when the number, z no menopauses impacts the number, x of operated menopauses in addition to the number, y of the natural menopauses. This is captured using (14) and (16). That is:

$$i_{(x,y)|z \rightarrow (x,y)} = \left\{ \frac{\rho_{(x,y)|z}}{s\rho_{(x,y)|z \rightarrow y}} \right\} = \frac{1}{1 + \sqrt{1 - \rho_{x,z}^2}} \tag{18}$$

Finally, of more concern to the healthcare agencies among the three counts: The number, x of operated menopauses, the number, y of the natural menopauses and the number, z no menopauses is the state of the incidence rate of the number, x of operated menopauses. In other words, is an estimated probability, θ for operated menopause is not negligible but rather significant? This is a hypothesis testing and it can be performed using the Likelihood Ratio Test (LRT) procedure. The LRT requires estimator of the parameters. The Maximum Likelihood Estimator (MLE) is preferable over others because of its *invariance property*. That is, the MLE of a function of the parameters is simply the function of the MLEs. We therefore, now, proceeds to obtain the MLE of the parameters in the *bivariate menopause distribution* (1).

Suppose that a *bivariate* random sample $(x_1, y_1), (x_2, y_2), \dots, (x_n, y_n)$ of size n is drawn from the *bivariate menopause distribution* (1). Then, the likelihood function is:

$$L(x_1, x_2, \dots, x_n, y_1, y_2, \dots, y_n | \phi, \theta, n) = (1 - \phi)^n \left(\frac{\phi}{1 - \phi} \right)^{\bar{x} + \bar{y}} \theta^{\bar{x}} (1 - \theta)^{\bar{y}} \prod_{i=1}^n \frac{n!}{x_i! y_i! (n - x_i - y_i)!} \tag{19}$$

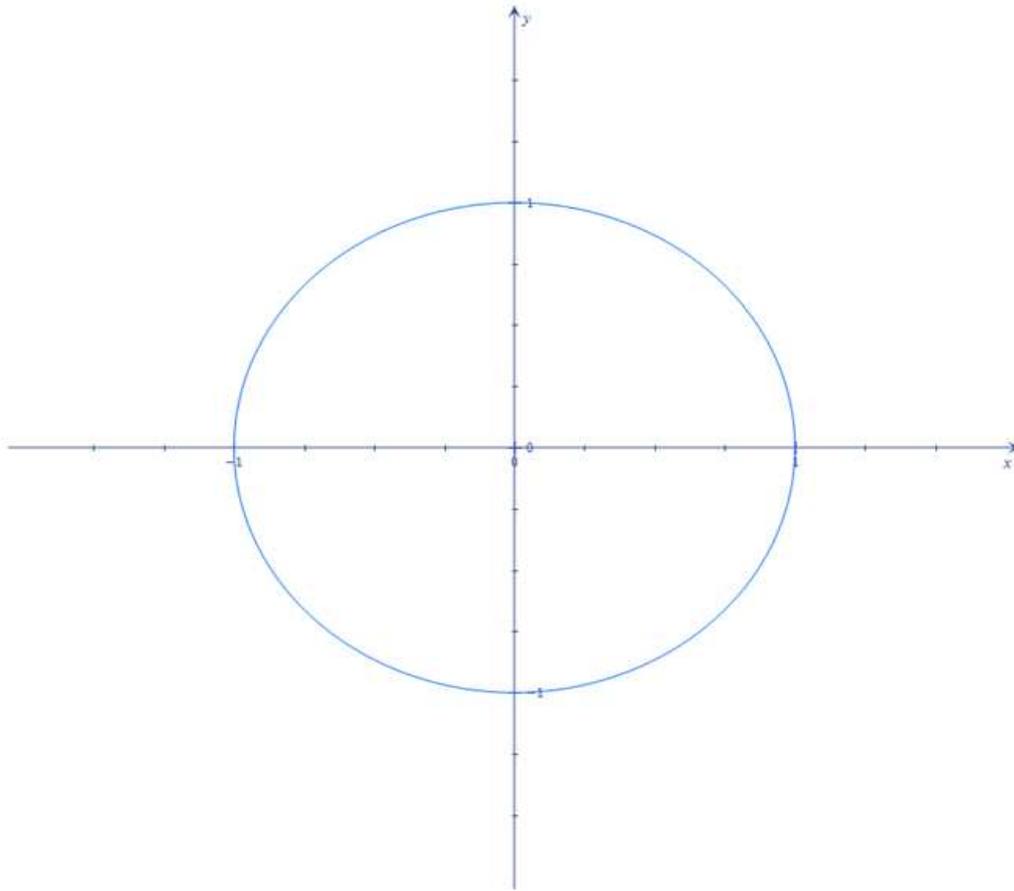


Fig. 2. Circular relationship $\rho_{x,z}^2 + \rho_{y,z}^2 = 1$ when $\rho_{x,y} = 0$

Equating the derivative of the logarithm of the likelihood (19) with respect to the parameters ϕ and θ to zero and solving them provides the MLEs (20) and (21). That is:

$$\hat{\phi}_{MLE} = \frac{(\bar{x} + \bar{y})}{n} \tag{20}$$

And:

$$\hat{\theta}_{MLE} = \frac{\bar{x}}{(\bar{x} + \bar{y})} = \frac{\bar{x}}{n\hat{\phi}_{MLE}} \tag{21}$$

A comment on (21) is worthwhile and that is when an estimate of the probability $(1 - \hat{\phi}_{MLE})$ for *no menopause* is larger, it is likely that the estimate of the probability $\hat{\theta}_{MLE}$ for *operated menopause* is also larger. To

test the null hypothesis $H_0 : \theta = \theta_0$ against the alternative hypothesis $H_1 : \theta > 0$, the likelihood ratio is:

$$\Lambda_o = \ln\{L(\theta_o, \hat{\phi}_{MLE}) / L(\hat{\theta}_{MLE}, \hat{\phi}_{MLE})\} \tag{22}$$

$$\approx \theta_o(\bar{x} - \bar{y}) + 2\left(\frac{1}{\bar{x}} + \frac{1}{\bar{y}}\right)^{-1} - \bar{x}$$

Which follows a chi-squared distribution with 1 Degrees of Freedom (DF) and non-centrality parameter:

$$\hat{\delta}_{\theta_o} = \left| \frac{(\hat{\theta}_{MLE} - \theta_o)}{\text{var}(\hat{\theta}_{MLE})} \right| \tag{23}$$

The $\text{var}(\hat{\theta}_{MLE})$ is a diagonal element in the *variance-covariance matrix*. Stuart and Ord (1994) for details:

$$\Sigma = \begin{bmatrix} \text{var}(\hat{\theta}_{MLE}) & \text{cov}(\hat{\theta}_{MLE}, \hat{\phi}_{MLE}) \\ \text{cov}(\hat{\theta}_{MLE}, \hat{\phi}_{MLE}) & \text{var}(\hat{\phi}_{MLE}) \end{bmatrix}$$

Which is inverse of the *information matrix*:

$$I = E \begin{bmatrix} -\partial_{\phi\phi}^2 \ln L & -\partial_{\phi\theta}^2 \ln L \\ -\partial_{\theta\phi}^2 \ln L & -\partial_{\theta\theta}^2 \ln L \end{bmatrix}$$

where, the notation L and E stand for the likelihood function and expectation respectively. Because $E(-\partial_{\phi\theta}^2 \ln L) = 0$, note that:

$$\text{var}(\hat{\theta}_{MLE}) = \bar{x}(\bar{x} + \bar{y})\bar{y}$$

Hence, the non-centrality (23) becomes:

$$\hat{\delta}_{\theta_0} = \left| \frac{(1-\theta_0) - \frac{\theta_0}{\bar{x}}}{(\bar{x} + \bar{y})^2} \right| \tag{24}$$

The central rather than the non-central chi-squared is popularly tabulated. To make use of the central chi-squared table, why not apply the property that a non-central chi-squared with 1 DF and non-centrality parameter, δ is equivalent to $(1 + \frac{\delta}{1+\delta})$ times the central chi-squared with $\frac{(1+\delta)^2}{(1+2\delta)}$ DF. It means then that the null hypothesis $H_0 : \theta = \theta_0$ is rejected in favor of the alternative hypothesis $H_1 : \theta > 0$ with a p-value in (25):

$$p\text{-value} = \Pr \left[\chi^2_{\frac{(1+\delta_0)^2}{(1+2\delta_0)}} > \left\{ 1 + \frac{\left(\frac{1-\theta_0}{\bar{y}} - \frac{\theta_0}{\bar{x}} \right)}{\left(\bar{x} + \bar{y} + \frac{1-\theta_0}{\bar{y}} - \frac{\theta_0}{\bar{x}} \right)} \right\} \left\{ \theta_0(\bar{x} - \bar{y}) + 2\left(\frac{1}{\bar{x}} + \frac{1}{\bar{y}} \right)^{-1} - \bar{x} \right\} \right] \tag{25}$$

where, $\hat{\delta}_{\theta_0}$ is as specified in (24).

The power of the LRT is the probability of accepting the true specific alternative hypothesis $H_1: \theta = \theta_1 > 0$. That is:

$$\text{power} = \Pr \left[\chi^2_{\frac{(1+\delta_1)^2}{(1+2\delta_1)}} < \left\{ 1 + \frac{\left(\frac{1-\theta_0}{\bar{y}} - \frac{\theta_0}{\bar{x}} \right)}{\left(\bar{x} + \bar{y} + \frac{1-\theta_0}{\bar{y}} - \frac{\theta_0}{\bar{x}} \right)} \right\} \left\{ \theta_0(\bar{x} - \bar{y}) + 2\left(\frac{1}{\bar{x}} + \frac{1}{\bar{y}} \right)^{-1} - \bar{x} \right\} \right] \chi^2_{\frac{(1+\delta_0)^2}{(1+2\delta_0)}, \alpha} \tag{26}$$

$$\left[\frac{\left\{ 1 + \frac{\left(\frac{1-\theta_1}{\bar{y}} - \frac{\theta_1}{\bar{x}} \right)}{\left(\bar{x} + \bar{y} + \frac{1-\theta_1}{\bar{y}} - \frac{\theta_1}{\bar{x}} \right)} \right\} \left\{ \theta_1(\bar{x} - \bar{y}) + 2\left(\frac{1}{\bar{x}} + \frac{1}{\bar{y}} \right)^{-1} - \bar{x} \right\}}{\left\{ 1 + \frac{\left(\frac{1-\theta_0}{\bar{y}} - \frac{\theta_0}{\bar{x}} \right)}{\left(\bar{x} + \bar{y} + \frac{1-\theta_0}{\bar{y}} - \frac{\theta_0}{\bar{x}} \right)} \right\} \left\{ \theta_0(\bar{x} - \bar{y}) + 2\left(\frac{1}{\bar{x}} + \frac{1}{\bar{y}} \right)^{-1} - \bar{x} \right\}} \right]$$

where, the non-centrality $\hat{\delta}_{\theta_1}$ is:

$$\hat{\delta}_{\theta_1} = \left| \frac{(1-\theta_1) - \frac{\theta_1}{\bar{x}}}{(\bar{x} + \bar{y})^2} \right| \tag{27}$$

3. ILLUSTRATION WITH MACMAHON AND WORCESTER DATA ON MENOPAUSE

In this section, the developments of the previous section are illustrated using Macmahon and Worcester (1966) data in. Realizing that the age is an important factor in discussions of menopause data, their data are split in terms of those in age below 40 years in the **Table 1**, those in the age bracket (40, 50) in the **Table 2** and those above 50 years in the **Table 3**. The age, number x of operative menopauses, the number y of natural menopauses, the number z of no menopauses and the sample sizes n of 7, 10 and 9 women are displayed in the **Table 1** through 3 respectively.

The MLE $\hat{\phi}_{MLE}$ in (20) of the probability for a menopause to occur is displayed for all three groups in **Table 4** and it is small (that is 0.06) for those below 40 years, only 0.369 for those in (40, 50) years, larger (that is 0.93) for those above 50 years. It is interesting that the MLE $\hat{\phi}_{MLE}$ in (21) of the probability for a woman to

undergo an operational menopause is displayed in **Table 4** and it is larger (that is 0.92) for those in below 40 years, only 0.57 for those in (40-50) years and smaller (that is 0.32) for those above 50 years. The proportionality for x and y within those who menopause are displayed in **Fig. 5-7** and they mean that the proportionality for x diminishes from those below 40 years to those in (40, 50) years and then to those above 50 years. Are the MLE $\hat{\theta}_{MLE}$ in (21) of the probability for a woman to undergo an operational menopause is negligible (that is, the null hypothesis is $H_0 : \theta = \theta_0 = 0.01$)? To answer the question, the p-value of the LRT in (25) is calculated and displayed for all three groups in **Table 4**. Note that the p-value is small for those below 40 years and for those above 50 years but not for those in (40, 50) years. How likely the LRT would accept the true alternative hypothesis $H_1 : \theta = \theta_1 = 0.8$? Using the expression (26) for the power, it is calculate and displayed for all three groups in **Table 4** and they are 0.99 suggesting that the LRT is quite powerful.

How correlated are the number, x of the operative menopauses and the number, y of the natural menopauses is? Using (9), the correlation $\hat{\rho}_{x,y}$ is calculated for the three groups and displayed in **Table 4** suggesting that it is weak (that is 0.09) for those below 40 years, larger (that is 0.91) for those in (40, 50) years, but negative (that is - 0.53) for those above 50 years.

The correlation level $\hat{\rho}_{x,z}$ between the number, x of the operative menopauses and the number, z of the no menopauses is calculated using (12) and displayed in the **Table 4**. The correlation is positive and small (that is 0.32) for those below 40 years, larger (that is 0.5) for those above 50 years but negative and smallest (that is - 0.38) for those in (40, 50) years. This pattern does not exist in the correlation between y and z .

The correlation is negative and smallest (that is -0.68) for those in (40, 50) years, negative and larger (that is - 0.52) for those below 40 years but positive and largest (that is 0.14) for those above 50 years. The correlation level $\hat{\rho}_{y,z}$ between the number, y of the natural menopauses and the number, z of the no menopauses is calculated using (13) and displayed in the **Table 4**.

After an adjustment of the impact of the number, z of the no menopauses on the number, x of the operative menopauses and on the number, y of the natural menopauses, how much are the correlation between the number, x of the operative menopauses and the number, y of the natural menopauses? This is partial correlation. Using (14), the partial correlation $\hat{\rho}_{(x,y)|z}$ is estimated and displayed in the **Table 4** and the numbers suggest that it is negative (that is -0.71) for those above 50 years, medium (that is 0.42) for those below 40 years but largest (that is 0.96) for those in (40, 50) years.

Table 1. Menopause among those below 40 years old in Macmahon and Worcester (1966)

Case	Age	X (operative menopause)	Y (natural menopause)	Z (non menopausal)	N (women sampled)
1	27.50	4.00	0.00	376.00	380.00
2	32.50	21.00	0.00	338.00	359.00
3	35.50	7.00	0.00	82.00	89.00
4	36.50	5.00	0.00	82.00	87.00
5	37.50	5.00	1.00	55.00	61.00
6	38.50	11.00	2.00	70.00	83.00
7	39.50	11.00	2.00	86.00	99.00
Mean	35.35	9.14	0.71	155.57	165.42
Variance	17.14	35.47	0.90	19161.95	19602.62

Table 2. Menopause among those in 40-50 years old in Macmahon and Worcester (1966)

Case	Age	X (operative menopause)	Y (natural menopause)	Z (non menopausal)	N (women sampled)
8	40.50	8.00	1.00	69.00	78.00
9	41.50	7.00	1.00	58.00	66.00
10	42.50	16.00	4.00	60.00	80.00
11	43.50	11.00	5.00	58.00	74.00
12	44.50	10.00	3.00	54.00	67.00
13	45.50	20.00	12.00	67.00	99.00
14	46.50	16.00	11.00	49.00	76.00
15	47.50	18.00	16.00	41.00	75.00
16	48.50	19.00	18.00	43.00	80.00
17	49.50	20.00	19.00	27.00	66.00
Mean	46.50	16.29	12.00	48.43	76.71
Variance	4.67	17.57	38.67	168.60	121.20

Table 3. Menopause among those in above 50 years old in Macmahon and Worcester (1966)

Case	Age	X (operative menopause)	Y (natural menopause)	Z (non menopausal)	N (women sampled)
18	50.5	18.000	32.00	22.00	72.00
19	51.5	10.000	38.00	18.00	66.00
20	52.5	16.000	30.00	8.00	54.00
21	53.5	18.000	40.00	9.00	67.00
22	54.5	18.000	28.00	4.00	50.00
23	55.5	19.000	25.00	1.00	45.00
24	56.5	13.000	36.00	1.00	50.00
25	57.5	13.000	40.00	1.00	54.00
26	58.5	13.000	33.00	0.00	46.00
Mean	55.5	15.710	33.14	3.43	52.29
Variance	4.67	7.238	34.14	13.60	54.24

Table 4. Comparison across age groups

Statistics	Below 40 years	In (40-50) years	Above 50 years
Corr (x, y)	0.090	0.914	-0.530
Corr (x, z)	0.320	-0.380	0.501
Corr (y, z)	-0.520	-0.680	0.140
Partial corr (x, y) in (14)	0.320	0.960	-0.700
Partial corr (x, y) in (15)	0.270	0.700	-0.700
Partial corr (x, y) in (16)	0.300	0.890	-0.600
Index of y in (17)	0.510	0.520	0.540
Index of x in (18)	0.540	0.580	0.500
$\hat{\phi}_{MLE}$	0.059	0.369	0.934
$\hat{\theta}_{MLE}$	0.927	0.576	0.322
p-value with $\theta_0 = 0.01$	0.003	0.120	0.020
power with $\theta_1 = 0.8$	0.990	0.990	0.990

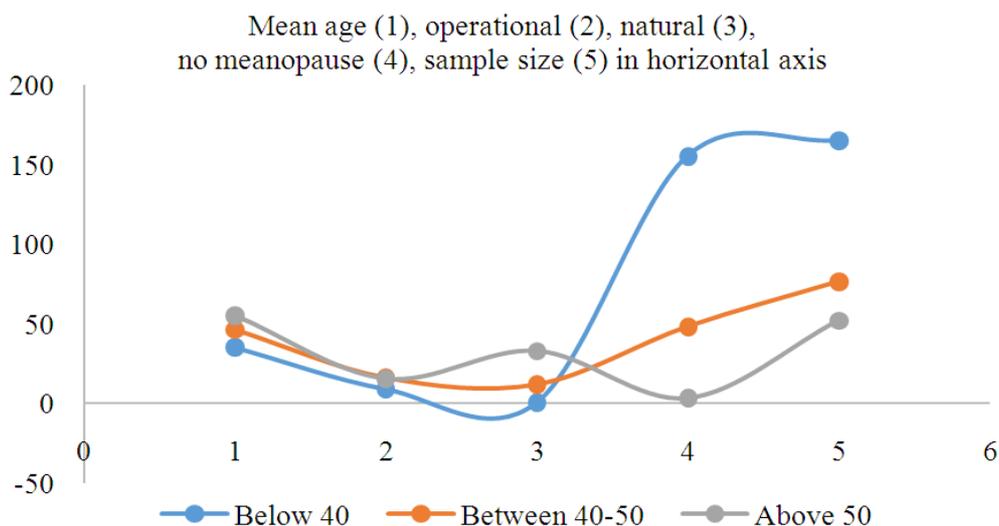


Fig. 3. Comparison of mean age, x, y, z and n in <40, between 40-50 and >50 years

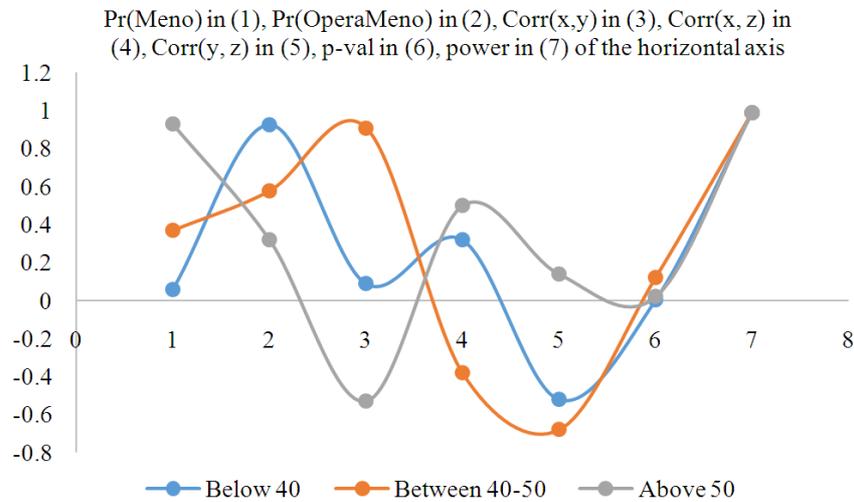


Fig. 4. Comparisons among the three groups: Below 40, between 40-50 and above 50 years

Blue area=Pr(Operational Menopause)
Red =Pr(Natural Menopause) among below 40
years old



Fig. 5. For <40 years

Blue area=Pr(Operational Menopause)
Red =Pr(Natural Menopause) among
above 50 years old



Fig. 7. For >50 years

Blue area=Pr(Operational Menopause)
Red =Pr(Natural Menopause) among
(40-50) years old



Fig. 6. For (40-50) years

If an adjustment of the impact of the number, z of the no menopauses on the number, x of the operative menopauses but on the number, y of the natural menopauses, how much are the correlation between the number, x of the operative menopauses and the number, y of the natural menopauses? This is called semi-partial correlation. Using (15), the semi-partial correlation $s\hat{\rho}_{(x,y)|z \rightarrow x}$ is estimated and displayed in the **Table 4** and the numbers suggest that it is negative (that is -0.7) for those above 50 years, medium (that is 0.27) for those below 40 years but largest (that is 0.7) for those in (40, 50) years. This trend continues in the semi-partial correlation $s\hat{\rho}_{(x,y)|y}$.

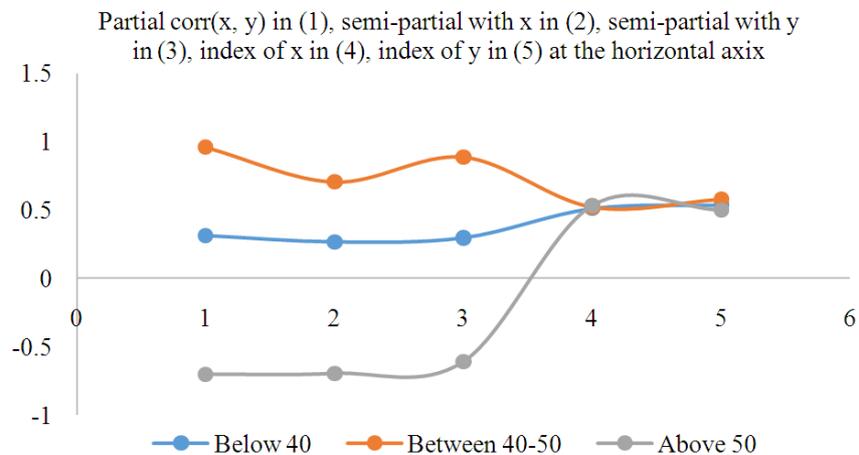


Fig. 8. Partial correlations and indices

If an adjustment of the impact of the number, z of the no menopauses on the number, y of the natural menopauses but on the number, x of the operative menopauses, how much are the correlation between the number, x of the operative menopauses and the number, y of the natural menopauses? This is called semi-partial correlation. Using (16), the semi-partial correlation $s\hat{\rho}_{(x,y)y}$ is estimated and displayed in the **Table 4** and the numbers suggest that it is negative (that is -0.6) for those above 50 years, medium (that is 0.30) for those below 40 years but largest (that is 0.89) for those in (40, 50) years.

The *index of increase*, $i_{(x,y)|z \rightarrow (x,y)}$ in the relationship between the number, x of operated menopauses and the number, y of the natural menopauses when the number, z no menopauses impacts the number, y of the natural menopauses in addition to the number, x of operated menopauses, according to (17), is displayed in **Table 4**. The numbers are consistently around the value 0.52 in its domain $[0, 1]$.

The *index of increase*, $i_{(x,y)|z \rightarrow (x,y)}$ in the relationship between the number, x of operated menopauses and the number, y of the natural menopauses is when the number, z no menopauses impacts the number, x of operated menopauses in addition to the number, y of the natural menopauses, according to (18), is displayed in **Table 4**. The numbers are consistently around the value 0.54 in its domain $[0, 1]$.

These infrastructures among the number x of operated menopauses, the number y of the natural menopauses and the number z of the no menopauses are captured graphically in **Fig. 3, 4 and 8** for the sake of easy and comprehensive understanding.

4. CONCLUSION

It was not clear how the operative, natural and no menopauses are triangularly connected. With the assistance of the new *bivariate menopause distribution* (1) and the statistical expressions which are derived in this article, several intriguing triangular relations among the operative, natural and no menopauses become possible. In this process, a lesson is learned and it is that the age factor is not after all a preserver of the trends. Are there better predictors of the incidences of the operative, natural and no menopauses? Do pertinent data exist out there? If so, there is a research need to develop a suitable multiple linear regression methodology for such data.

5. ACKNOWLEDGMENT

The researcher wishes to thank *Kathir Selvan Shanmugam* for bringing the data in **Table 1 to 3** to my attention.

6. REFERENCES

Al-Jawadi, Z.A.M., 2014. Thyroid hormones (T3 and T4) as a marker of uterine cancer risk factor after menopause. *Am. J. Applied Sci.*, 11: 857-859. DOI: 10.3844/ajassp.2014.857.859

Cheng, G., Y. Yuan and J. Liu, 1997. Relative contribution of ageing and menopause to the changes of lumbar bone density in 1,400 Beijing women. *Zhonghua Fu Chan Ke Za Zhi*, 32: 532-534. PMID: 9639752

- Crawford, S.L., 2000. Epidemiology: Methodologic Challenges in the Study of Menopause. In: Menopause: Biology and Pathobiology, Lobo, R.A., J. Kelsey and R. Marcus (Eds.), Academic Press, San Diego, ISBN-10: 0080536204, pp: 159-174.
- Hadjidakis, D., E. Kokkinakis and M. Sfakianakis, 1999. The type and time of menopause as decisive factors for bone mass changes. *Eur. J. Clin. Invest.*, 29: 877-885. DOI: 10.1046/j.1365-2362.1999.00541.x
- Harlow, B.L. and L.B. Signorello, 2000. Factors associated with early menopause. *Maturitas*, 35: 3-9. DOI: 10.1016/S0378-5122(00)00092-X
- Hu, F.B., F. Grodstein, C.H. Hennekens, G.A. Colditz and M. Johnson *et al.*, 1999. Age at natural menopause and risk of cardiovascular disease. *Arch. Int. Med.*, 159: 1061-1066. DOI: 10.1001/archinte.159.10.1061
- Jacobsen, B.K., S.F. Knutsen and G.E. Fraser, 1999. Age at natural menopause and total mortality and mortality from ischemic heart disease: The adventist health study. *J. Clin. Epidemiol.*, 52: 303-307. PMID: 10235170
- Joakimsen, O., K.H. Bonna, E. Stensland-Bugge and B.K. Jacobsen, 2000. Population-based study of age at menopause and ultrasound assessed carotid atherosclerosis: The Tromsø study. *J. Clin. Epidemiol.*, 53: 525-530. PMID: 10812326
- Luisetto, G., M. Zangari, F. Bottega, P. Galuppo and A. Nardi *et al.*, 1995. Different rates of forearm bone loss in healthy women with early or late menopause. *Osteoporos. Int.*, 5: 54-62. PMID: 7703625
- Macmahon, B. and J. Worcester, 1966. Age at Menopause, United States, 1960-1962. 1st Edn., U.S. Department of Health, Education and Welfare, Public Health Service, Washington, D.C., pp: 20.
- Main, C., B. Knight, T. Moxham, R. Gabriel Sanchez and L.M. Sanchez Gomez *et al.*, 2013. Hormone therapy for preventing cardiovascular disease in post-menopausal women. *Cochrane Database Syst. Rev.* PMID: 23633307
- Ohta, H., I. Sugimoto, A. Masuda, S. Komukai and Y. Suda *et al.*, 1996. Decreased bone mineral density associated with early menopause progresses for at least ten years: Cross-sectional comparisons between early and normal menopausal women. *Bone*, 18: 227-231. PMID: 8703577
- Orleans, R.J., L. Li, M.J. Kim, J. Guo and M. Sobhan *et al.*, 2014. FDA approval of paroxetine for menopausal hot flashes. *New Eng. J. Med.*, 370: 1777-1779. PMID: 24806158
- Osei-Hyiaman, D., T. Satoshi, M. Ueji, T. Hideto and K. Kano *et al.*, 1998. Timing of menopause, reproductive years and bone mineral density: A cross-sectional study of postmenopausal Japanese women. *Am. J. Epidemiol.*, 148: 1055-1061. PMID: 9850127
- Paganini-Hill, A., M.D. Krailo and M.C. Pike, 1984. Age at natural menopause and breast cancer risk: The effect of errors in recall. *Am. J. Epidemiol.*, 119: 81-85. PMID: 6691338
- Stuart, A. and J. Ord, 1994. Kendall's Advanced Theory of Statistics. 1st Edn., Griffin Publications, London.
- Tavani, A., E. Ricce, C. LaVecchia, M. Surace and G. Benzi *et al.*, 2000. Influence of menstrual and reproductive factors on ovarian cancer risk in women with and without family history of breast or ovarian cancer. *Int. J. Epidemiol.*, 29: 799-802. PMID: 11034959
- Treloar, A.E., 1981. Menstrual cyclicity and the premenopause. *Maturitas*, 3: 249-264. DOI: 10.1016/0378-5122(81)90032-3
- Van Der Schouw, Y.T., Y. Van Der Graaf, E.W. Steyerberg, E.W. Steyerberg and J.C. Eijkemans *et al.*, 1986. Age at menopause as a risk factor for cardiovascular mortality. *Lancet*, 347: 714-718. PMID: 8602000