Greetings & Hello to everyone!

Welcome to my presentation!

I am Ram Shanmugam

Please send comments to:

Dr. Ram Shanmugam

Professor, School of Health Administration

Texas State University, 601 University Drive

San Marcos, TX 78666, USA

E-mail: rs25@txstate.edu

Office phone: (512) 245 9772 Fax: (512) 245 8712

Topic of my presentation is ***Shortage, Illegal Trade, and Unmet Demand of Organ or Tissue Transplant***

- Some of these are published in an article:
- Ramalingam Shanmugam (2015) ***Journal of Epidemiology & Community Medicine, 1, 1, page 1-9.***

- What is organ or tissue transplantation?
- It is replacing a person's damaged or absent organ by an organ from a living or deceased person.
- The regenerative medicine allows sometimes to grow tissue from the person's own stem cells.
- Organs or tissues that are transplanted within the person's body are called auto grafts.
- Transplants that are performed between two subjects of the same species are called allografts.

A selective history

- The first and earliest historical transplant was auto grafted skin in nose reconstruction called *rhinoplasty* by an Indian surgeon Sushruta in the 2nd century B. C.
- Other noteworthy transplants and their time are now summarized.

- In 1905, a Czech Surgeon, Eduard Zirm performed the first successful cornea transplant.
- In 1950, an US surgeon, Richard H. Lawler performed the first successful kidney transplant.
- In 1967, the first successful heart transplant was done by a South Africa's surgeon Christian Barnard.
- In 2005, an Indian surgeon, P. N. Mhatre did the first successful ovarian transplant.

What are popular transplants?

- Popularly transplanted organs are heart, kidneys, liver, lungs, pancreas, intestine, and thymus.
- Commonly transplanted tissues are bones, cornea, skin, heart valves, nerves and veins.
- Tissue is procured from those who experienced brain death or cessation of heartbeat.
- Unlike organs, tissues are stored for a short duration, up to five years.
- The American Association of Tissue Banks estimates that a million tissue transplants occur each year in the United States of America (USA).
- Bone marrow is a flexible tissue in the interior of bones. Bone marrow constitutes a four percent of the total body mass of humans, supporting the body's immune system.

A selective history (continues)

- There are about 25 million people are listed as bone marrow donors worldwide.
- A practical difficulty in transplants is the recipient's body rejection of organ/tissue due to antigens.
- This is resolved using a technique called serotyping, which checks the matching between the recipient and the donor.
- The World Health Organization (WHO) announced that about 66,000 kidney transplants, 21,000 liver transplants and 6,000 heart transplants were performed globally in 2005.
- Still, there is a severe shortage of organs or tissues. A purchase or sale of illegal organs from live donors is prohibited in many countries.

Stumbles for transplant

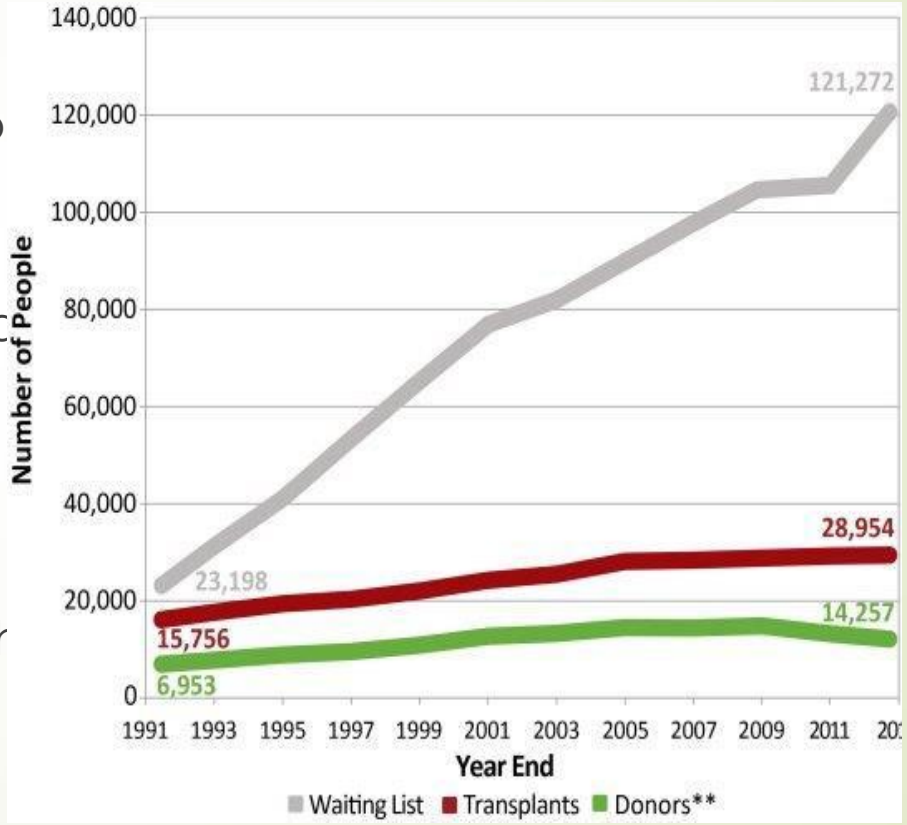
- For a variety of reasons, thousands of persons are waiting for organ transplant.
- This number has been rising globally over the years, while the number of donors is quite stable.
- The supply of organs comes from the living or dead persons on voluntarily basis. Of course, the number of donors is trailing far behind the demand for organ transplant.
- The awareness to donate organs to use ought to increase so that their gap narrows.
- There might be cultural, religious, ethnic, or economic stumbles for not many donated organs for transplant.
- At the same time, one wonders whether the demand for organ increases due to deteriorating health among world citizens due to environmental, genetic, or poor quality life practices.
- A promotion of healthy living might reduce the need for organ transplant.

Facts

- For a lack of organs, about 22 people die every day.
- An average of 81 transplants occurs every day in USA. Another person is added to the waiting list in every 10 minutes.
- About 123,000 people are waiting for an organ transplant. The year 2014 was a record- breaking year for the number of transplants performed and the number of deceased donor transplants.
- In 2014, about 29,532 transplants occurred.
- Only 23,715 transplants were from deceased donors.
- About 3,500 heart transplants are performed annually worldwide. The majority of these (about 2,300) are performed annually in the USA.

Additional facts and interpret

- A single lung transplant takes about eight hours, while a doub lung transplant takes about twelve hours to complete.
- A heart-lung transplant is carriec out to replace both heart and lungs in a single operation.
- The figure 1 illustrates that there a wider gap between the number waiting for organ and th number donors of organ.



An explanation

- The number of persons who received transplants is more than the number of donors.
- Does this hint out the under-reporting of data occasionally, family members or friends to alleviate the suffering of loved ones donate organs and it may be not reported.
- The number waiting for organ transplant is much higher than the number of organ donors and it suggests a shortage for organ transplant.
- The number of organ donors is lesser than the number of recipients and it suggests that there must have been illegal organ trade [2].
- The number waiting for organ transplant is higher than the number of recipients and it suggests the existence of unmet demand.

Hence,

- We develope a statistical methodology to extract and interpret data information and then compute a confidence interval for
  - shortage,
  - illegal trade, and
  - unmet demand

with respect to organ transplantation.

- About 80 percent of all organs are donated and used in the same geographic area.
- Many patients travel to countries, where organs are obtainable through commercial transactions.
- The unlicensed international organ trade is forbidden.

What does WHO mention?

- World Health Organization (WHO) urges nation to protect poor and vulnerable groups from undue exploitation of organ/tissue theft.
- Medical tourists travel to poor countries seeking cheap and illegal organ purchase.

Evidences

- The number waiting for organ is about 700 percent more than the number of donors, which is only 46 percent of the number of recipients.
- How is that more recipients exist than the number of donors.
- The number of donors must have been under- reported.
- Close relatives or friends could have donated organ to wipe out the suffering of those recipients. Such a donation is legal but should be reported.

- Questions:
  - Q1: The gap between the number of donors and the number of recipients is the data evidence for the existence of illegal transactions of organ trade. Is the gap statistically significant?
  - Q2: The gap between the number waiting for organ and the number of donors is *shortage* of organs for transplant. Is it statistically significant?
  - Q3: The gap between the number waiting for organ and the number of recipients indicates an *unmet demand for organ transplant*. Is the gap statistically significant?
  - Q4: Conditional on the removal of illegal organ trade (that is, $YR = YD$), what might be the expected and volatility of organ shortage?

To understand data information,

- First step is an appropriate model for the data.
- What is a model?
- Model is an abstraction of reality.
- Statistical methodology is constructed based on the model.

- Benefits are:
  - For the importance of policy changes to encourage organ transplantation.
  - The beneficiaries of organ transplantation would certainly have a higher quality life.

Notations & model

- *YW* , *YR* , and *YD* represent the number of persons waiting, the number of recipients, and the number of donors respectively.
- Because of the large data size and the well-known *central limit theorem,* the random vector $\underline{Y}$ follows a *trivariate Gaussian distribution*
-

Trivariate Normal

$$N_3(\underline{\mu}_{3x1}, \underline{\underline{\Sigma}}_{3x3}) = \frac{1}{\sqrt{2\pi|\underline{\underline{\Sigma}}|}} e^{-(\underline{y}-\underline{\mu})'\underline{\underline{\Sigma}}^{-1}(\underline{y}-\underline{\mu})} \quad (1)$$

$$, \underline{\underline{\Sigma}}_{3x3} = \begin{pmatrix} \sigma_W^2 & \sigma_{WR} & \sigma_{WD} \\ \sigma_{WR} & \sigma_R^2 & \sigma_{RD} \\ \sigma_{WD} & \sigma_{RD} & \sigma_D^2 \end{pmatrix},$$

Mahalanobis distance

their Gaussianity. The Mahalanobis distance is a Euclidean distance of an observed mean $\underline{\mu}_{3x1}$ adjusted three-dimensional vector $(\underline{y} - \underline{\mu})$ from the origin $\underline{0}_{3x1}$.

- MLEs

$$\underline{\hat{\mu}}_{3x1} = \begin{pmatrix} \hat{\mu}_W \\ \hat{\mu}_R \\ \hat{\mu}_D \end{pmatrix} = \begin{pmatrix} \overline{y}_W \\ \overline{y}_R \\ \overline{y}_D \end{pmatrix}, \qquad (2)$$

$$\hat{\underline{\Sigma}}_{3x3} = \begin{pmatrix} \hat{\sigma}_W^2 & \hat{\rho}_{WR}\hat{\sigma}_W\hat{\sigma}_R & \hat{\rho}_{WD}\hat{\sigma}_W\hat{\sigma}_D \\ \hat{\rho}_{WR}\hat{\sigma}_W\hat{\sigma}_R & \hat{\sigma}_R^2 & \hat{\rho}_{RD}\hat{\sigma}_R\hat{\sigma}_D \\ \hat{\rho}_{WD}\hat{\sigma}_W\hat{\sigma}_D & \hat{\rho}_{RD}\hat{\sigma}_R\hat{\sigma}_D & \hat{\sigma}_D^2 \end{pmatrix}$$

How to answer the questions?

- To answer the questions, we nee to develop a new statistical methodology.
- For this purpose, let us provoke c statistical property of multivariat Gaussian distribution.
- That is, a contrast transformation, $G = CY$ follows a multivariate Gaussian,

$N_p(\underline{C}_{px3}\underline{\mu}_{3x1}, \underline{C}_{px3}{}'\underline{\Sigma}^{-1}_{3x3}\underline{C}_{3xp})$ where $\underline{C}_{px3}$ is a chosen matrix of p number of independent contrast coefficients and the inverse $\underline{\Sigma}^{-1}_{3x3}$ of the symmetric variance-covariance matrix is

$$\underline{\Sigma}^{-1}_{3x3} = \frac{1}{[1+2\rho_{WR}\rho_{WD}\rho_{RD} - (\rho^2_{WR}+\rho^2_{WD}+\rho^2_{RD})]} \begin{pmatrix} \frac{(1-\rho^2_{RD})}{\sigma^2_W} & \frac{(\rho_{WD}\rho_{RD}-\rho_{WR})}{\sigma_W\sigma_R} & \frac{(\rho_{WR}\rho_{RD}-\rho_{WD})}{\sigma_W\sigma_D} \\ \frac{(\rho_{WD}\rho_{RD}-\rho_{WR})}{\sigma_W\sigma_R} & \frac{(1-\rho^2_{WD})}{\sigma^2_R} & \frac{(\rho_{WR}\rho_{WD}-\rho_{RD})}{\sigma_R\sigma_D} \\ \frac{(\rho_{WR}\rho_{RD}-\rho_{WD})}{\sigma_W\sigma_D} & \frac{(\rho_{WR}\rho_{WD}-\rho_{RD})}{\sigma_R\sigma_D} & \frac{(1-\rho^2_{WR})}{\sigma^2_D} \end{pmatrix} \quad (4)$$

Making results for the gaps

matrix. How much of this distance is covered by a contrast, $G = \underline{C}\underline{Y}$ is $\underline{\bar{y}}'\{\underline{C}'\hat{\Sigma}^{-1}\underline{C}\}\underline{\bar{y}}$. Hence, a relative could be created to indicate the significance of the covered Mahalanobis distance and it is the ratio

$$\delta = \frac{\underline{\bar{y}}'\{\underline{C}'\Sigma^{-1}\underline{C}\}\underline{\bar{y}}}{\underline{\bar{y}}'\hat{\Sigma}^{-1}\underline{\bar{y}}}$$

. This relative index is indicative of higher significance.

We now examine the validity of the research hypothesis Q1. For this purpose, we select $\underline{C}_{1x3} = (0,1,-1)$. Consequently, an observed *illegal organ trade level* $G_1 = Y_R - Y_D$ follows a *univariate Gaussian distribution* with mean $\hat{\mu}_{G_1} = \bar{y}_R - \bar{y}_D$ and variance

$$\sigma^2_{G_1} = \frac{[(1+2\rho_{WR}\rho_{WD}\rho_{RD}) - (\rho^2_{WR} + \rho^2_{WD} + \rho^2_{RD})]}{\left[\frac{(1-\rho^2_{WR})}{\sigma^2_D} + \frac{(1-\rho^2_{WD})}{\sigma^2_R} + 2\frac{\rho_{RD|W}\sqrt{(1-\rho^2_{WR})(1-\rho^2_{WD})}}{\sigma_R\sigma_D}\right]} \quad (5)$$

Confidence interval for illegal organ trade

fixed number waiting for organ. Hence, a $100(1-\alpha)$ percent *confidence interval* for the unobserved *illegal organ trade* or *organ wastage level* is

$$\bar{y}_R - \bar{y}_D \pm z_{\alpha/2}\hat{\sigma}_{G_1} \qquad (6)$$

Based on (5). How significant is the contrast transformation, G_1 It is indicated by the ratio $\hat{\delta}_{G_1} = \frac{(\bar{y}_R - \bar{y}_D)^2}{\hat{\sigma}^2_{G_1}(\underline{\bar{y}}'\hat{\Sigma}^{-1}\underline{\bar{y}})}$. The domain for the relative is

Organ shortage

number recipient for organ. Hence, a $100(1-\alpha)$ percent *confidence interval* for the unknown *organ shortage gap* is

$$\bar{y}_W - \bar{y}_D \pm z_{\alpha/2}\hat{\sigma}_{G_2} \qquad (8)$$

According to (7). How significant is the contrast transformation, G_2 It is indicated by the index ratio

$\hat{\delta}_{G_2} = \dfrac{(\bar{y}_W - \bar{y}_D)^2}{\hat{\sigma}^2_{G_2}(\underline{\bar{y}}'\hat{\Sigma}^{-1}\underline{\bar{y}})}$. The domain for the relative is

- Where

$$\sigma^2_{G_2} = \frac{[(1+2\rho_{WR}\rho_{WD}\rho_{RD}) - (\rho^2_{WR}+\rho^2_{WD}+\rho^2_{RD})]}{\left[\dfrac{(1-\rho^2_{WR})}{\sigma^2_D} + \dfrac{(1-\rho^2_{RD})}{\sigma^2_W} + 2\dfrac{\rho_{WD|R}\sqrt{(1-\rho^2_{WR})(1-\rho^2_{DR})}}{\sigma_W\sigma_D}\right]} \qquad (7)$$

Unmet organ demand

fixed number of organ donors. Hence, a $100(1-\alpha)$ percent *confidence interval* for the unobserved *unmet demand for organ* is

$$\bar{y}_W - \bar{y}_R \pm z_{\alpha/2}\hat{\sigma}_{G_3} \qquad (10)$$

Using (9). How significant is the contrast transformation G_3? It is indicated by the ratio

$$\hat{\delta}_{G_3} = \frac{(\bar{y}_W - \bar{y}_R)^2}{\hat{\sigma}^2_{G_3}(\underline{\bar{y}}'\hat{\Sigma}^{-1}\underline{\bar{y}})}$$

$$\sigma^2_{G_3} = \frac{[(1+2\rho_{WR}\rho_{WD}\rho_{RD}) - (\rho^2_{WR}+\rho^2_{WD}+\rho^2_{RD})]}{\left[\frac{(1-\rho^2_{WD})}{\sigma^2_R} + \frac{(1-\rho^2_{RD})}{\sigma^2_W} + 2\frac{\rho_{WR|D}\sqrt{(1-\rho^2_{WD})(1-\rho^2_{RD})}}{\sigma_W\sigma_R}\right]} \qquad (9)$$

To answer Q4, when

there is no illegal organ trade suggesting that $Y_R = Y_D$

random vector (Y_W, Y_R) is a *bivariate Gaussian distribution*

$$N_2(\underline{\mu}_{2x1}, \underline{\Sigma}_{2x2}) = \frac{1}{\sqrt{2\pi|\Sigma|}} e^{-(\underline{y}-\underline{\mu})'\underline{\Sigma}^{-1}(\underline{y}-\underline{\mu})}, \quad (11)$$

With $\underline{\mu}_{2x1} = \begin{pmatrix} \mu_W \\ \mu_R \end{pmatrix}, \underline{\Sigma}_{2x2} = \begin{pmatrix} \sigma_W^2 & \sigma_{WR} \\ \sigma_{WR} & \sigma_R^2 \end{pmatrix}$,

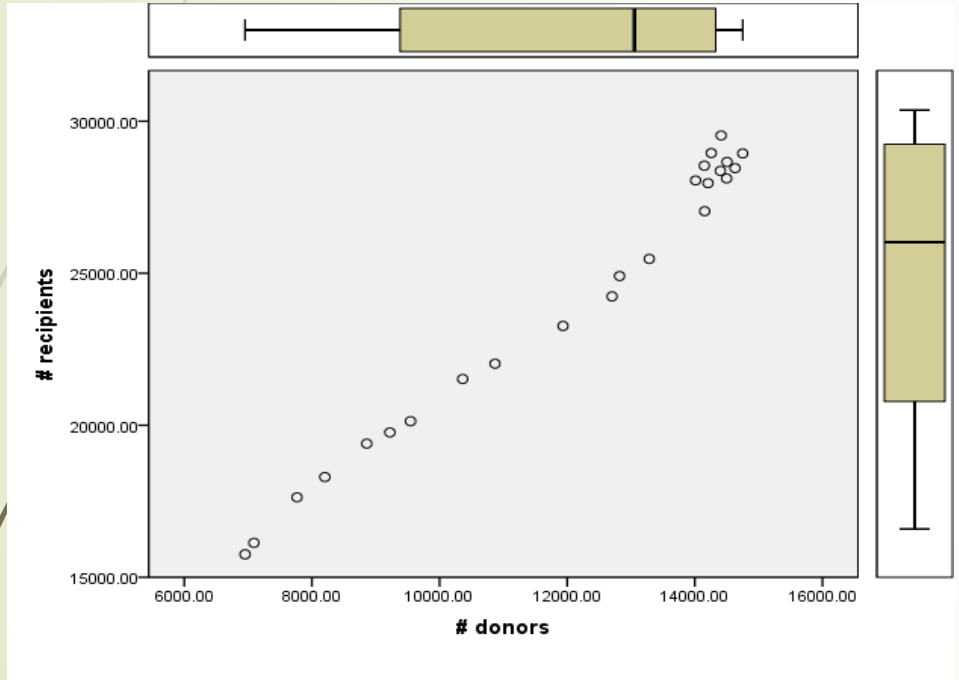
waiting and the number of recipients. Hence, a 100(1-α) percent *confidence interval* for the unobserved *unmet demand for organ* in the absence of illegal organ trade and waste of organs is

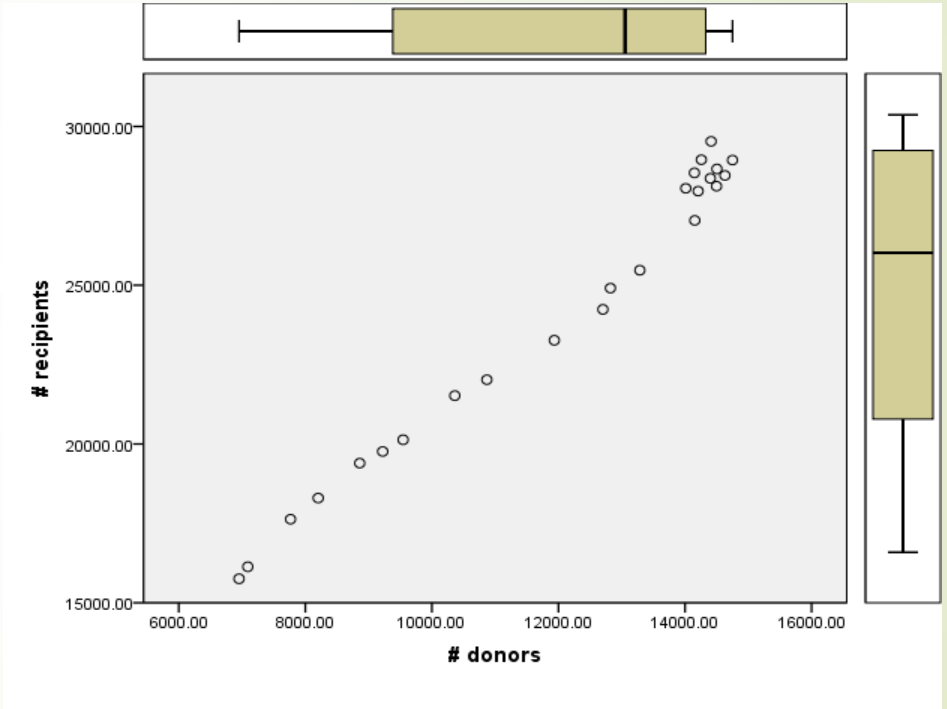
$$\bar{Y}_W - \bar{Y}_R \pm z_{\alpha/2}\hat{\sigma}_{G_4}. \quad (14)$$

How significant is the contrast transformation G_4? It is indicated by the ratio

$$\hat{\delta}_{G_4} = \frac{(\bar{y}_W - \bar{y}_R)^2(\hat{\sigma}_W^2 + 2\hat{\rho}_{WR}\hat{\sigma}_W\hat{\sigma}_R + \hat{\sigma}_R^2)}{(\hat{\sigma}_W^2\bar{y}_W^2 - 2\hat{\rho}_{WR}\hat{\sigma}_W\bar{y}_W\hat{\sigma}_R\bar{y}_R + \hat{\sigma}_R^2\bar{y}_R^2)}. \quad (15)$$

Illustration using WHO data on worldwide transplants during 1991-2013





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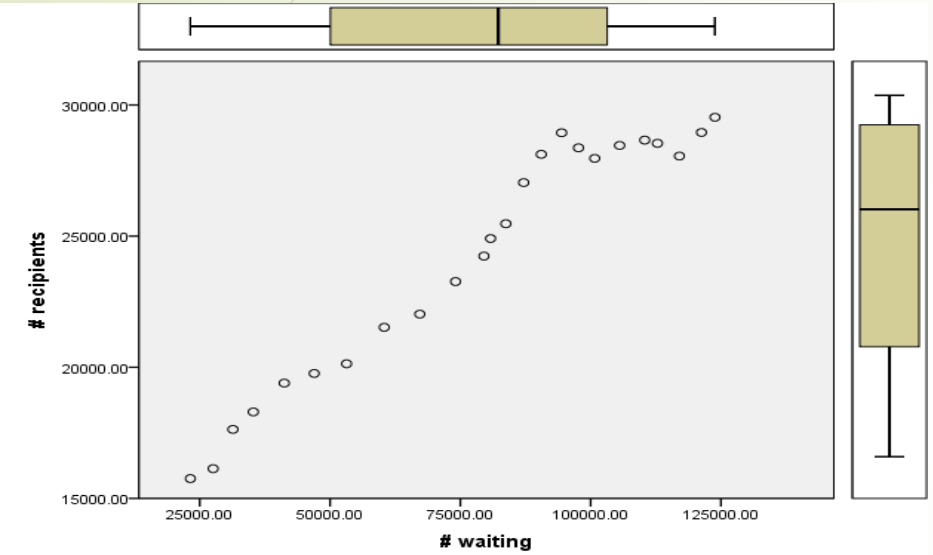

Correlation	Waiting number, Y_W	Number of recipients Y_R	Number of donor, Y_D
Waiting number, Y_W	$r_{WW} = 1$	$r_{WR} = 0.97$	$r_{WD} = 0.95$
Number of recipients Y_R	$r_{RW} = 0.97$	$r_{RR} = 1$	$r_{RD} = 0.99$
Number of donor, Y_D	$r_{DW} = 0.95$	$r_{DR} = 0.99$	$r_{DD} = 1$

Unmet organ demand

According (10), a 95 percent *confidence interval* for the unobserved *unmet demand for organ* in the period 1991-2013 is (53,628, 55,433) worldwide. The relative index, $\hat{\delta}_{G_3}$ in the expansion of the Mahalanobis' distance for the *unmet demand for organ* in the period 1991-2013 is only 75.51, with a reasonable higher significance.

Organ shortage

According (8), a 95 percent *confidence interval* for the unobserved *organ shortage* in the period 1991-2013 is (65,023, 66,504) worldwide. The relative index, $\hat{\delta}_{G_2}$ in the expansion of the Mahalanobis' distance for the *organ shortage* in the period 1991-2013 is only 163.12, with much higher significance.

Illegal organ trade

distance of 185.88. According (6), a 95 percent *confidence interval* for the unobserved *illegal organ trade* or *organ wastage level* in the period 1991-2013 is (10,691, 11, 774) worldwide. The relative index, $\hat{\delta}_{G_1}$ in the expansion of the Mahalanobis' distance for the *illegal organ trade* or *organ wastage level* in the period 1991-2013 is only 8.88, with not much of higher significance.

If illegal organ trade is abolished,

hypothetical situation of total abolishment of *illegal organ trade* or *organ wastage*, according (14), a 95 percent *confidence interval* for the unobserved *unmet demand for organ* in the period 1991-2013 would be (50,552, 58,509) worldwide. This confidence interval under an abolishment of *illegal organ trade* is wider than what would that otherwise. Paradoxically, the presence of *illegal organ trade* helps. However, the relative index, $\hat{\delta}_{G_4}$ in the expanded Mahalanobis' distance shrinks to 0.16 for the *unmet demand for organ* in the period 1991-2013, with a drastically significant reduction. These findings become possible with the help of the statistical methodology in Section2.

In conclusion,

- More awareness needs to me made among the potential organ donors about the importance of donating organs.
- Worldwide facilities ought to be established and supported to procure organs soon enough from those who unexpectedly die due to accidents or heart attack.
- Priorities should be given to air transport the procured organs to the correct destination for transplanting them in those waiting for organs in a world of heavy traffic with congestions.
- In addition, stocking and preservation of unutilized organs should be encouraged for future implantation.
- The WHO ought to provide a leadership to promote and implement the above mentioned incentives among the nations.

Conclusion continues

- Times of India, on 31 July 2015 announced that the Indian Air Force (IAF) allowed its special aircraft, an Embraer, for a unique operation for transporting a kidney and a liver from Pune to Delhi to save the life of two critically-ill patients.
- This incidence cites the importance of promoting the importance of a quick air transporting organ or tissue from a remote place to a destination place worldwide.
- No forced donation must be allowed.
- Humans have a pair of organs. A human can live with just one organ. An illusionary tendency might exist to sell off one of the organ pairs for a high price.
- The market value of a kidney, a liver, and a heart are $100,000, $250,000, and $860,000 respectively.

Conclusion continues

- Thank you for your attention!
- I appreciate your comments!
- Please send me your thoughts via e-mail rs25@txstate.edu .
- Bye now!!