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Stochastic Analysis with Simulation of Time to Hospitalization and Hospitalization Time for Diabetes with 1 out of 2 Defective Organs-Failure and Coxian-2 Observation Time for Prophylactic Treatment

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Abstract

This paper assumes that a diabetic person has two defective organs A and B where organ A is exposed to failure due to a two phase risk process and organ B has a general failure time. Prophylactic treatment starts after one or two observations following Coxian-2 distribution. In the model, the hospitalization for diabetes starts when any one of the defective organs A or B fails or when prophylactic treatment starts. The joint transform of the distribution of time to hospitalization for treatment and hospital treatment time are presented along with their expectations. Numerical examples are presented. Simulation studies are under taken using linear congruential generators. Erlang-Coxian 2 distribution is considered for the general distribution of life time of organ B. Cyclic two-phase and Erlang distributions are considered for hospital stage treatment times. Random values of all the variables are generated to present simulated values of time to hospitalization and hospital treatment times for various parameter values of Coxian time to start prophylactic treatment.

Keywords: Time to Prophylactic treatment, PH 2 cyclic distribution, Erlang-Coxian2 distribution, Simulation study, Linear congruential generator.

Introduction

In real life situations, prevention of the disease is given very much importance as that would prevent loss of life. Observation of the patient by experts before hospital

admission for treatment is absolutely required to safe guard and protect the health and interest of the patient in providing proper treatment. In addition to regular observation by experts, at times seeking second opinion by another team of experts may be necessary for providing treatment. Thus two different observation times, namely, one for routine observation and another one for second opinion in complicated cases are required for resolving issues during treatment. Several issues on risk factors of diabetes mellitus have been analyzed by Bhattacharya S. K., Biswas R., Ghosh M. M., and Banerjee in [1]. Foster D. W., Fauci A. S., Braunward E., Isselbacher K. J., Wilson J. S., Mortin J. B and Kasper D. L have studied diabetes mellitus in [2]. Kannell W. B and McGee D. L[3] have presented Diabetes and Cardiovascular Risk Factors. King H, Aubert R. E and Herman W. H in [4] have concentrated on the global burden of diabetes during the period 1995-2025. Mathematical studies have been undertaken by Usha and Eswariprem in [5] where they have focused their research on the models with metabolic disorder. Eswariprem, Ramanarayanan and Usha [6] have analyzed such models with prophylactic treatment for prevention of the disease. Mathematical studies on diabetic models with prophylactic treatment will be very beneficial to the society. Moreover cure from the disease after treatment is time consuming and above all is seldom achieved in many cases. This paper concentrates on situations of prophylactic treatment with a second opinion (second observation) if necessary for proper treatment of the disease when one organ A of the patient is exposed to failure due to a two phase failure process and his another organ B fails after a random time. Rajkumar, Gajivaradhan and Ramanarayanan [7] have treated recently a diabetic model with one observation time where time to admit for prophylactic treatment has exponential distribution. They have also discussed the effect of prophylactic treatment. Since the random variable assumed in [7] being exponential has constant hazard rate, it may be useful if the hazard rate changes to another level after some time so that mean time to admit for prophylactic treatment changes and the models studied in [7] provide only one observation time which forces hospital admission after that. In some real life situations and in many complicated cases second opinion or consultation by another medical team is sought for, necessitating another observation time to provide perfect treatment. In this paper the time to admit for prophylactic treatment is assumed to have Coxian 2 distribution and this distribution has been identified for providing two observation times respectively for the first opinion and for the second opinion if sought for special cases. Probabilistic arguments and simulation techniques are utilized for the presentation of the results. Analyzing real life stochastic models researchers do collect data directly from the hospitals (primary data) or use secondary data from research organizations or use simulated data for studies. Simulation studies are more suitable in this area since in most of the cases in general, hospitable real life data may not be sufficiently available and at times they may heavily depend on the biased nature of the data collectors. They may vary hospital to hospital and they may not be genuine enough for the study since many other factors such as the quality of nursing and medical treatments provided to the patients by hospitals are involved. The alertness of the patients in expressing the symptoms and timely assistance of insurance and finance agencies involved may play always the leading role in providing proper treatment.

These are necessary to generate perfect and genuine data. Since the reputation of many connected organizations are involved, there may not be anybody to take the responsibility of the perfectness of the data provided. In this area not much of significant simulation studies are available or under taken so far at any depth. For simulation analysis, models with general random variables present real life-like situations and results. It is well known that any general distribution may be well approximated by Erlang-Coxian 2 (EC) Phase type distribution and the details of the same are presented by T. Osogami and M. H. Balter [8] by the method of comparison of first three moments. For the simulation analysis here, Martin Haugh [9] results and Law and Kelton methods using Hull and Dobell results [10] are utilized to generate uniform random values and all other random values required. In the model treated here, the person is provided treatment when any one of the defective organs A or B fails or when he is admitted for prophylactic treatment (PT). Depending on the values of the parameter of time to PT two types, namely, type (i) unequal holding rates and type (ii) equal holding rates for observation times are noticed and studied. The joint Laplace-Stieltjes transform of time to hospitalization for treatment (T) and hospital treatment time (H), their individual distributions, the expected T and the expected H for the model are derived. Numerical examples are presented assuming exponential life time for the organ B. Simulation studies are provided assuming organ A has two phase life time distribution, organ B has EC life time, Coxian time to PT, Erlang and phase-two cyclic hospital treatment times. Varying the parameter of time to PT several simulated values are generated for T and H.

Model : 1-out-of 2 Organs Failure and Prophylactic Treatment

The general assumptions of the model are given below considering the patient has two defective organs A and B.

Assumptions

(1) Defective organ A producing insulin functions in two phases of damaged levels, namely, damaged level 1 (phase 1) and damaged level 2 (phase 2) where level 1 is considered to be a better level of the two with lesser failure rate. Due to pre-hospital medication the organ A may move to level 1 from level 2 and due to negligence it may move to level 2 from level 1. The failed level of the organ A is level 3. The transition rates of the organ A to the failed level 3 from level 1 and from level 2 are respectively $\lambda_1 and\ \lambda_2\ with\ \lambda_2 > \lambda_1$. The transition rates from level 1 to level 2 is μ_1 and from level 2 to level 1 is μ_2. At time 0, the organ A is level 1 and let F_A denote its life time (time to failure).

(2) Defective organ B has a general life time F_B with Cumulative distribution function (Cdf) $F_B(x)$.

(3) Independent and irrespective of the status of the organs A and B, the patient may be admitted for prophylactic treatment (PT) in a random observation time F_P with Coxian 2 Cdf. The observation time F_P has exponential distribution with parameter α (exp(α)) with probability q (one observation only) and with

probability p=1-q the observation time is the sum of two random times (two observations) with exp(α) and exp(β).

(4) The hospitalization begins when any one of the two organs fails or when PT starts.

(5) The hospital treatment time of the organ A, the treatment time of the organ B and the PT time in the hospital are random variables $H_1, H_2 and\ H_3$ with Cdfs $H_1(x), H_2(x)$ and $H_3(x)$ respectively.

Analysis

To study the model two Cdfs of F_A and F_P, namely, F_A(x) and F_P(x), are to be obtained. They are derived now.

Derivation of Cdf F_A(x) of Time to Failure of Organ A from the Level 1 at Time 0

Levels 1 and 2 of the organ A may be considered as phases 1 and 2 respectively of PH phase 2 type distribution.

Considering the failed state as absorbing state 3,

$$Q=\begin{bmatrix} -(\lambda_1+\mu_1) & \mu_1 & \lambda_1 \\ \mu_2 & -(\lambda_2+\mu_2) & \lambda_2 \\ 0 & 0 & 0 \end{bmatrix} \quad (1)$$

is the infinitesimal generator describing the transitions. Various transition probabilities may be derived as follows. Before failure (absorption) the organ A may be in any state 1 or 2. Let for i, j=1, 2 $P_{i,j}(t)$=P (At time t the organ A is in level j and it has not failed during (0, t) | at time 0 it is in level i). (2)

The probability $P_{1,1}(t)$ may be written considering the two possibilities that without a failure (i) the organ A may remain in level 1 during (0, t) or (ii) it moves to level 2 at time u for u ∈ (0, t) and it is in level 1 at time t. It may be seen that

$$P_{1,1}(t) = e^{-(\lambda_1+\mu_1)t} + \int_0^t \mu_1\, e^{-(\lambda_1+\mu_1)u}\, P_{2,1}(t-u)\, \mathrm{du}. \quad (3)$$

Using similar arguments it may be seen that

$$P_{2,1}(t) = \int_0^t \mu_2\, e^{-(\lambda_2+\mu_2)u}\, P_{1,1}(t-u)\, \mathrm{du}, \quad (4)$$

$$P_{1,2}(t) = \int_0^t \mu_1\, e^{-(\lambda_1+\mu_1)u}\, P_{2,2}(t-u)\, \mathrm{du} \quad (5)$$

and $P_{2,2}(t) = e^{-(\lambda_2+\mu_2)t} + \int_0^t \mu_2\, e^{-(\lambda_2+\mu_2)u}\, P_{1,2}(t-u)\, \mathrm{du}.$ (6)

The above four equations (3) to (6) may be solved using Laplace transform method to obtain results as follows.

$$P_{1,1}(t) = (\tfrac{1}{2})\, e^{-at}(e^{bt}+e^{-bt}) + (\tfrac{1}{4b})\,(\lambda_2-\lambda_1+\mu_2-\mu_1)\, e^{-at}(e^{bt}-e^{-bt}) \quad (7)$$

$$P_{1,2}(t)=(\tfrac{\mu_1}{2b})\, e^{-at}(e^{bt}-e^{-bt}) \quad (8)$$

$$P_{2,2}(t) = (\tfrac{1}{2})\, e^{-at}(e^{bt}+e^{-bt}) + (\tfrac{1}{4b})\,(\lambda_1-\lambda_2+\mu_1-\mu_2)\, e^{-at}(e^{bt}-e^{-bt}) \quad (9)$$

$$P_{2,1}(t)=(\tfrac{\mu_2}{2b})\, e^{-at}(e^{bt}-e^{-bt}) \quad (10)$$

Here

$$a=(\tfrac{1}{2})\,(\lambda_1+\lambda_2+\mu_1+\mu_2) \text{ and } b=(\tfrac{1}{2})\,\sqrt{(\lambda_1-\lambda_2+\mu_1-\mu_2)^2+4\mu_1\mu_2}. \quad (11)$$

It can be seen that $a^2 - b^2 = \lambda_1\lambda_2 + \lambda_1\mu_2 + \lambda_2\mu_1$;
$(\frac{a+b-\lambda_1}{2b})$ (a-b)= $\left(\frac{a^2-b^2-a\lambda_1}{2b}\right) + \frac{\lambda_1}{2} = \frac{\lambda_1}{2} + \frac{\lambda_1}{4b}(\lambda_2 - \lambda_1 + \mu_2 - \mu_1) + (\frac{\lambda_2\mu_1}{2b})$ and
$(\frac{a-b-\lambda_1}{2b})$ (a + b)=$-\frac{\lambda_1}{2} + \frac{\lambda_1}{4b}(\lambda_2 - \lambda_1 + \mu_2 - \mu_1) + (\frac{\lambda_2\mu_1}{2b})$ (12)
The absorption to state 3 can occur from any phase 1 or 2 since the organ A may fail from levels 1 or 2. The probability density function (pdf) $p_{1,3}(t)$ of time to failure of the organ A, starting from level 1 at time 0 is written using the absorption rates from levels 1 and 2 as follows. For convenience let $p_{1,3}(t) = f_A(t)$. After simplification using the above results
$p_{1,3}(t) = \lambda_1 P_{1,1}(t) + \lambda_2 P_{1,2}(t) = f_A(t) = k_1$(a-b) $e^{-(a-b)t} - k_2$(a + b) $e^{-(a+b)t}$ (13)

where $k_1 = \frac{a+b-\lambda_1}{2b}$ and $k_2 = \frac{a-b-\lambda_1}{2b}$.
The Cdf of F_A is $F_A(t) = \int_0^t f_A(u)$du=1 $-k_1\, e^{-(a-b)t} + k_2\, e^{-(a+b)t}$. (14)

Derivation of Cdf F_P(x) of Time to Admit the Person for Prophylactic Treatment (PT)
Noting the first observation time (state 1 holding time) has exp(α) and with probability p the second observation is provided where the observation time (state 2 holding time) has exp(β) and considering the absorbing state as 3, the infinitesimal generator describing the various transitions is given by

$$Q' = \begin{bmatrix} -\alpha & p\alpha & q\alpha \\ 0 & -\beta & \beta \\ 0 & 0 & 0 \end{bmatrix}. \quad (15)$$

The pdf of time to hospitalization for PT starting from state1 is
f_P(t)=$q\alpha e^{-\alpha t} + \int_0^t p\alpha\, e^{-\alpha u}\, \beta e^{-\beta(t-u)} du.$
On integration two types are noticed, namely, type (i) unequal holding rates α ≠ β and type (ii) equal holding rates

$$\alpha=\beta.\ f_P(t) = \begin{cases} k_1'\beta e^{-\beta t} + k_2'\alpha e^{-\alpha t}, if\ \alpha \neq \beta \text{ type (i)} \\ q\alpha e^{-\alpha t} + p\alpha^2 t\, e^{-\alpha t}, if\ \alpha = \beta\ type\ (ii) \end{cases} \quad (16)$$

$$F_P(t) = \begin{cases} 1 - k_1' e^{-\beta t} - k_2' e^{-\alpha t}, if\ \alpha \neq \beta\ type\ (i) \\ 1 - e^{-\alpha t} - p\alpha\, t\, e^{-\alpha t}, if\ \alpha = \beta\ type\ (ii) \end{cases} \quad (17)$$

is Cdf of time to PT, where $k_1' = \frac{p\alpha}{(\alpha-\beta)}$ and $k_2' = \frac{(q\alpha-\beta)}{(\alpha-\beta)}$. To study the model the joint pdf of two variables (T, H) where the variable T, the time to hospitalization, is the minimum of {the absorption time of PH phase 2 (Organ A failure time), the failure time of organ B, the time to PT} and the variable H is the hospitalization time where H=$H_1 or\ H_2 or\ H_3$ according as the treatment begins when Organ A fails or when organ B fails or when the patient is admitted for PT respectively. Let $\bar{V}$(x)=1 – V(x) for any function V(x). The joint pdf of (T, H) is
f (x, y)=$f_A(x)\,\overline{F_B}(x)\,\overline{F_P}(x)h_1(y) + \overline{F_A}(x)f_B(x)\,\overline{F_P}(x)h_2(y)$
$+ \overline{F_A}(x)\,\overline{F_B}(x)f_P(x)h_3(y)$ (18)

The first term of the RHS of (18) is the pdf-part that the organ A fails before the failure of the organ B and before the completion of the time to PT and the hospitalization is provided for the failure of the organ A. The second term is the pdf-part that the organ B fails before the failure of organ A and before the completion of the time to PT and the hospitalization is provided for the failure of the organ B. The third term is the pdf-part that the patient is admitted for PT before the failures of organ A and organ B and the PT is provided. The double Laplace transform of the pdf of (T, H) is given by

$f^*(\xi, \eta)=\int_0^\infty \int_0^\infty e^{-\xi x-\eta y}$ f(x, y) dx dy. (19)

Here * indicates Laplace transform. The equation (19) using the structure of equation (18) becomes a single integral.

$f^*(\xi, \eta)=\int_0^\infty e^{-\xi x}[f_A(x)\,\overline{F_B}\,(x)\overline{F_P}\,(x)h_1^*(\eta) + \overline{F_A}(x)f_B(x)\,\overline{F_P}\,(x)h_2^*(\eta) + \overline{F_A}(x)\overline{F_B}\,(x)f_P(x)h_3^*(\eta)\,]\,dx.$ (20)

From (16) and (17) equation (20) has to be written for $\alpha \neq \beta$ and $\alpha=\beta$.

Model Type (i): Results for Unequal Holding Rates $\alpha \neq \beta$

It can be seen after simplification, equation (20) becomes using (13), (14), (16) and (17) for type (i) as $f^*(\xi, \eta)=[\ k_1k_1'(a-b)\ \overline{F_B}^*\ (a-b+\beta+\xi)+\ k_1k_2'(a-b)\ \overline{F_B}^*(a-b+\alpha+\xi)-k_2k_1'(a+b)\ \overline{F_B}^*(a+b+\beta+\xi)-k_2k_2'\ (a+b)\ \overline{F_B}^*(a+b+\alpha+\xi)]\ h_1^*(\eta)\ +\ [\ k_1k_1'f_B^*\ (a-b+\beta+\xi)\ +\ k_1k_2'\ f_B^*\ (a-b+\alpha+\xi)-k_2k_1'f_B^*\ (a+b+\beta+\xi)-k_2k_2'\ f_B^*\ (a+b+\alpha+\xi)]\ h_2^*(\eta)\ +\ [\ k_1k_1'\ \beta\ \overline{F_B}^*(a-b+\beta+\xi)\ +\ k_1k_2'\alpha\ \overline{F_B}^*(a-b+\alpha+\xi)-k_2k_1'\ \beta\overline{F_B}^*(a+b+\beta+\xi)-k_2k_2'\ \alpha\ \overline{F_B}^*(a+b+\alpha+\xi)]\ h_3^*(\eta).$ (21)

The Laplace transform of the pdf of T may be obtained after simplification by taking $\eta=0$ in equation (21). Noting that $f_B^*(s)=1-s\ \overline{F_B^*}(s)$ and $k_1k_1'+\ k_1k_2'-k_2k_1'-k_2k_2'=1$, it can be seen that $f^*(\xi, 0)=1-k_1k_1'\xi\ \overline{F_B}^*\ (a-b+\beta+\xi)-k_1k_2'\xi\ \overline{F_B}^*\ (a-b+\alpha+\xi)\ +\ k_2k_1'\xi\ \overline{F_B}^*\ (a+b+\beta+\xi)\ +\ k_2k_2'\xi\ \overline{F_B}^*\ (a+b+\alpha+\xi).$ (22)

Mean time to hospitalization is $E(T)=-\frac{d}{d\xi} f^*(\xi, 0)\,|_{\xi=0}$. This gives, $E(T)=k_1k_1'\ \overline{F_B}^*\ (a-b+\beta)\ +\ k_1k_2'\ \overline{F_B}^*\ (a-b+\alpha)-k_2k_1'\ \overline{F_B}^*\ (a+b+\beta)-k_2k_2'\ \overline{F_B}^*\ (a+b+\alpha).$ (23)

Using equation (21) the Laplace transform of the pdf of H may be obtained by taking $\xi=0$. $f^*(0, \eta)=k_1k_1'\ \overline{F_B}^*(a-b+\beta)\ [(a-b)\ h_1^*(\eta)\ +\ \beta\ h_3^*(\eta)-(a-b\ +\beta)\ h_2^*(\eta)]\ +\ k_1k_2'\ \overline{F_B}^*(a-b+\alpha)\ [(a-b)\ h_1^*(\eta)\ +\ \alpha\ h_3^*(\eta)-(a-b\ +\ \alpha)\ h_2^*(\eta)]-k_2k_1'\ \overline{F_B}^*(a+b+\beta)\ [(a+b)\ h_1^*(\eta)\ +\ \beta\ h_3^*(\eta)-(a+b+\beta)\ h_2^*(\eta)]-k_2k_2'\ \overline{F_B}^*(a+b+\alpha)\ [(a+b)\ h_1^*(\eta)\ +\ \alpha\ h_3^*(\eta)-(a+b+\alpha)\ h_2^*(\eta)]\ +\ h_2^*(\eta).$ (24)

Mean hospital treatment time is $E(H)=-\frac{d}{d\eta} f^*(0, \eta)\,|_{\eta=0}$. This gives $E(H)=k_1k_1'\ \overline{F_B}^*(a-b+\beta)\ [(a-b)\ E(H_1)+\ \beta\ E(H_3)-(a-b+\beta)\ E(H_2)]\ +\ k_1k_2'\ \overline{F_B}^*(a-b+\alpha)\ [(a-b)\ E(H_1)+\ \alpha\ E(H_3)-(a-b\ +\ \alpha)\ E(H_2)]-k_2k_1'\ \overline{F_B}^*(a+b+\beta)\ [(a+b)\ E(H_1)\ +\ \beta\ E(H_3)-(a+b+\beta)\ E(H_2)]-k_2k_2'\ \overline{F_B}^*(a+b+\alpha)\ [(a+b)\ E(H_1)\ +\ \alpha\ E(H_3)-(a+b+\alpha)\ E(H_2)]\ +\ E(H_2).$ (25)

Inversion of Laplace transform of (22) and (24) are straight forward. Noting P(T ≤ t)=L^{-1} ($\frac{f^*(\xi,0)}{\xi}$) and L^{-1} ($\frac{1-f_B^*(q+\xi)}{q+\xi}$) = L^{-1}($\overline{F_B}$ *(q + ξ))=e^{-qt} $\overline{F_B}$ (t), the Cdf of time to hospitalization T is P(T ≤ t)=F_T (t)=1-$k_1k_1'e^{-(a-b+\beta)t}$ $\overline{F_B}$ (t)−$k_1k_2'e^{-(a-b+\alpha)t}$ $\overline{F_B}$ (t) + $k_2k_1'e^{-(a+b+\beta)t}$ $\overline{F_B}$ (t) + $k_2k_2'e^{-(a+b+\alpha)t}$ $\overline{F_B}$ (t). (26)
The Cdf of H may be derived in the form given below. P (H ≤ t)=F_H (t)=k_1k_1' $\overline{F_B}$*$(a-b+\beta)$ [(a-b) $H_1(t)$+ β $H_3(t)$-(a-b + β) $H_2(t)$] + $k_1k_2'\overline{F_B}$*$(a-b+\alpha)$ [(a-b) $H_1(t)$+ α$H_3(t)$-(a-b + α) $H_2(t)$]-k_2k_1' $\overline{F_B}$*$(a+b+\beta)$ [(a + b) $H_1(t)$ + β $H_3(t)$-(a + b + β) $H_2(t)$]-k_2k_2' $\overline{F_B}$*$(a+b+\alpha)$ [(a + b) $H_1(t)$ + α $H_3(t)$-(a + b + α) $H_2(t)$] + $H_2(t)$. (27)

Model Type (ii): Results for Equal Holding Rates α=β.
It can be seen after simplification, equation (20) becomes using (13), (14), (16) and (17) for type (ii) as follows. f*(ξ, η)=[k_1(a-b) $\overline{F_B}$* $(a-b+\alpha+\xi)$ − k_2(a + b) $\overline{F_B}$* $(a+b+\alpha+\xi)$ − k_1(a-b) p α $\overline{F_B}$* ′$(a-b+\alpha+\xi)$ +k_2(a + b) p α $\overline{F_B}$*′$(a+b+\alpha+\xi)$] h_1^*(η) + [$k_1f_B^*(a-b+\alpha+\xi)-k_2f_B^*(a+b+\alpha+\xi)-k_1p\alpha f_B^{*\prime}(a-b+\alpha+\xi)+k_2p\alpha f_B^{*\prime}(a+b+\alpha+\xi)$] h_2^*(η) + [k_1 q α $\overline{F_B}$* $(a-b+\alpha+\xi)$ − k_2q α $\overline{F_B}$*$(a+b+\alpha+\xi)$ − k_1p α^2 $\overline{F_B}$*′ $(a-b+\alpha+\xi)$ + k_2 p α^2 $\overline{F_B}$*′$(a+b+\beta+\xi)$] h_3^*(η) (28)
where ′ indicates differentiation with respect to ξ. The Laplace transform of the pdf of T may be obtained after simplification by taking η=0 in equation (28), by noting that f_B^* (s)=1-s $\overline{F_B^*}$ (s) ; f_B^* ′(s)=-$\overline{F_B^*}$ (s)-s $\overline{F_B^*}$ ′(s) and by using $k_1 - k_2 = 1$ as follows.
f*(ξ, 0)=1-k_1ξ $\overline{F_B}$*$(a-b+\alpha+\xi)$ + k_2ξ $\overline{F_B}$*$(a+b+\alpha+\xi)$ + k_1p α ξ $\overline{F_B}$*′ $(a-b+\alpha+\xi)$ − k_2p α ξ $\overline{F_B}$*′$(a+b+\alpha+\xi)$ (29)
Mean time to hospitalization is E (T)=$-\frac{d}{d\xi}$ f*(ξ, 0) $|_{\xi=0}$. This gives,
E(T)=$k_1\overline{F_B}$*$(a-b+\alpha)$ − $k_2\overline{F_B}$*$(a+b+\alpha)$ − k_1p α $\overline{F_B}$*′ $(a-b+\alpha)$ + k_2p α $\overline{F_B}$*′$(a+b+\alpha)$. (30)
Using equation (28) the Laplace transform of the pdf of H may be obtained by taking ξ=0. f*(0, η)=[k_1(a-b) $\overline{F_B}$* $(a-b+\alpha)$ − k_2(a + b) $\overline{F_B}$* $(a+b+\alpha)$ − k_1(a-b) p α $\overline{F_B}$* ′$(a-b+\alpha)$ +k_2(a + b) p α $\overline{F_B}$*′$(a+b+\alpha)$] h_1^*(η) + [$k_1f_B^*(a-b+\alpha)-k_2f_B^*(a+b+\alpha)-k_1p\alpha f_B^{*\prime}(a-b+\alpha)+k_2p\alpha f_B^{*\prime}(a+b+\alpha)$] h_2^*(η) + [k_1 q α $\overline{F_B}$* $(a-b+\alpha)$ − k_2q α $\overline{F_B}$*$(a+b+\alpha)$ − k_1p α^2 $\overline{F_B}$*′ $(a-b+\alpha)$ + k_2 p α^2 $\overline{F_B}$*′$(a+b+\alpha)$] h_3^*(η). This after simplification becomes f*(0, η)=h_2^*(η) + k_1 $\overline{F_B}$* $(a-b+\alpha)$ [(a-b) h_1^*(η) + q α h_3^*(η)-(a-b + α-p α) h_2^*(η)]-k_2 $\overline{F_B}$* $(a+b+\beta)$[(a + b) h_1^*(η) + q α h_3^*(η)-(a + b + α-p α) h_2^*(η)]-k_1p α $\overline{F_B}$*′$(a-b+\beta)$ [(a-b) h_1^*(η) + α h_3^*(η)-(a-b + α) h_2^*(η)] + k_2p α $\overline{F_B}$*′$(a+b+\beta)$ [(a + b) h_1^*(η) + α h_3^*(η)-(a + b + α) h_2^*(η)] (31)
Expected treatment time can be written by replacing h_j^*(η) by E (H_j) for j=1, 2, 3 on the right side and using E (H)=$-\frac{d}{d\eta}$ f*(0, η) $|_{\eta=0}$. It may be seen E (H)=E(H_2) + k_1 $\overline{F_B}$* $(a-b+\alpha)$ [(a-b) $E(H_1)$ + q α $E(H_3)$-(a-b + q α) $E(H_2)$]-k_2 $\overline{F_B}$* $(a+b+\alpha)$ [(a + b) $E(H_1)$ + q α $E(H_3)$-(a + b + q α) $E(H_2)$]-k_1p α $\overline{F_B}$*′$(a-b+\alpha)$ [(a-b) $E(H_1)$

+α $E(H_3)$-(a-b + α) $E(H_2)$] + k_2p α $\overline{F_B}^{*\prime}(a+b+\alpha)$ [(a + b) $E(H_1)$ +α $E(H_3)$-(a + b + α) $E(H_2)$] . (32)

Inversion of Laplace transform of (29) and (31) are straight forward. Noting P(T ≤ t)=L^{-1} ($\frac{f^*(\xi,0)}{\xi}$); $L^{-1}(\overline{F_B}^*(q+\xi))=e^{-qt}\ \overline{F_B}$ (t) and $L^{-1}(\overline{F_B}^{*\prime}(q+\xi))$=-t $e^{-qt}\ \overline{F_B}$ (t), the Cdf of T is seen as P (T ≤ t)=F_T (t)=1-k_1 $e^{-(a-b+\alpha)t}\ \overline{F_B}(t)$ + $k_2\ e^{-(a+b+\alpha)t}\overline{F_B}(t) - k_1$p α t $e^{-(a-b+\alpha)t}\ \overline{F_B}(t)$ +k_2p α t $e^{-(a+b+\alpha)t}\ \overline{F_B}(t)$. (33)

From equation (31), P(H ≤ t)=F_H (t)=$H_2(t)$ + $k_1\ \overline{F_B}^*(a-b+\alpha)$ [(a-b) $H_1(t)$ + q α $H_3(t)$-(a-b +q α) $H_2(t)$]-$k_2\ \overline{F_B}^*(a+b+\alpha)$ [(a + b) $H_1(t)$ + q α $H_3(t)$-(a + b +q α) $H_2(t)$]-k_1p α $\overline{F_B}^{*\prime}(a-b+\alpha)$ [(a-b) $H_1(t)$ + α $H_3(t)$-(a-b + α) $H_2(t)$] + k_2p α $\overline{F_B}^{*\prime}(a+b+\alpha)$ [(a + b) $H_1(t)$ + α $H_3(t)$-(a + b + α) $H_2(t)$]. (34)

Special Cases of Life Times of Organ B:

Two special cases for organ B with (1) exponential life time and (2) EC life time distribution are considered below.

Special Case (1): Exponential Life Time for Organ B

When the life time of the organ B has exp(θ) then F_B(x)=1-$e^{-\theta x}$. E(T) and E(H) can be written using (23), (30), (25) and (32) for the two types (i) and (ii) by substituting $\frac{1}{\theta+s}$ for $\overline{F_B}$*(s) and $\frac{-1}{(\theta+s)^2}$ for $\overline{F_B}$*' (s).

Special Case (2): Erlang-Coxian 2 (EC) Life Time for Organ B

Let the life time of the organ B have EC distribution with parameter set (k, θ, θ_1, p_1, θ_2) which is the Cdf of the sum of Erlang (k, θ) and Coxian-2 (θ_1, p_1, θ_2) random variables where the Erlang part has k phases with parameter θ and the Coxian 2 has the infinitesimal generator describing the transition as

$$Q''=\begin{bmatrix} -\theta_1 & p_1\theta_1 & q_1\theta_1 \\ 0 & -\theta_2 & \theta_2 \\ 0 & 0 & 0 \end{bmatrix} \quad (35)$$

for $p_1 + q_1$=1 with starting phase 1. By comparing Q" with Q' in (15) the pdf of Coxian 2 may be written as $g_1(x) = (\frac{q_1\theta_1-\theta_2}{\theta_1-\theta_2})\ \theta_1 e^{-\theta_1 x} + (\frac{p_1\theta_1}{\theta_1-\theta_2})\theta_2 e^{-\theta_2 x}$ and $G_1(x)$=1-($\frac{q_1\theta_1-\theta_2}{\theta_1-\theta_2}$) $e^{-\theta_1 x}$-($\frac{p_1\theta_1}{\theta_1-\theta_2}$)$e^{-\theta_2 x}$. The Laplace transform of the Coxian 2 is $g_1^*(s) = (\frac{q_1\theta_1-\theta_2}{\theta_1-\theta_2})(\frac{\theta_1}{\theta_1+s})+(\frac{p_1\theta_1}{\theta_1-\theta_2})(\frac{\theta_2}{\theta_2+s})$. (36)

The Cdf F_B(x) of life time of organ B is the Cdf of the sum of Erlang and Coxian 2. So the Laplace transform of its pdf is f_B*(s)=$(\frac{\theta}{\theta+s})^k g_1^*(s)$ (37)

Using the fact $\overline{F_B}$(x)=1-F_B(x), the Laplace transform of $\overline{F_B}$(x) is obtained from (36) and (37) as follows. $\overline{F_B}$*(s)=$\frac{1-(\frac{\theta}{\theta+s})^k[(\frac{q_1\theta_1-\theta_2}{\theta_1-\theta_2})(\frac{\theta_1}{\theta_1+s})+(\frac{p_1\theta_1}{\theta_1-\theta_2})(\frac{\theta_2}{\theta_2+s})]}{s}$. (38)

The expected time to hospitalization and expected hospitalization time respectively E(T) and E(H) may be written considering equation (38) and its derivative and using (23), (30), (25) (32) for the two types (i) and (ii).

Numerical and Simulation Studies

(I) Numerical Studies:

As an application of the results obtained numerical study is taken up to present E(T) and E(H) for various values of the parameters introduced for the two types (i) and (ii) assuming $\lambda_1 = .3,\ \lambda_2 = .35, \mu_1 = .4, \mu_2 = .5$. Then from (11), a=0. 775; b=0. 45345893; a + b=1. 228458929; a-b=0. 321541071 which gives the life time of organ A has Cdf, F_A (t)=1-1. 02375195 $e^{-(0.321541071)\,t}$+ 0. 02375195$e^{-(1.228458929)t}$ with pdf f_A (t)=(0. 3291783001) $e^{-(0.3215410713)\,t}$-(0. 291783001) $e^{-(1.228458929)t}$. Let the organ B have Cdf of life time F_B (t)=1-$e^{-\theta t}$ with θ=0. 4, 0. 5, 0. 6 and 0. 7. Let the parameter of the Coxian time to PT for type (i) be with parameters α=0. 05, p=0. 2, 0. 4, 0. 6, 0. 8 and β=0. 1. Let the parameters for type (ii) be α=β=0. 1 with same values for p=0. 2, 0. 4, 0. 6, 0. 8. Fixing p=0. 2 calculations are done by varying θ as=0. 4, 0. 5, 0. 6 and 0. 7. Fixing θ=0. 4 calculations are done by varying p as=0. 2, 0. 4, 0. 6 and 0. 8. Let the expected values of various types of treatment times be E(H_1)=. 1, E(H_2)=0. 05 and E(H_3)=0. 005. For the two types (i) α ≠ β and (ii) α=β, E (T) and E (H) values are presented in tables 1 and 2. Out of θ and p, fixing one and varying the other, unidirectional variations on the expected values of E(T) and E(H) are noticed in the two tables presented here for the types (i) and (ii). The parameter values are substituted to obtain the statistical estimates. They present exact values of the estimates. Although θ and p cause variations in the value of E(T) and E(H) as seen here but do not present any sample-runs or real life situations. The effects of the life times of organs A, B, the effect of the time to PT and the effects of various treatments times can be studied only by simulating the situations. In simulation studies one may find real life like situations.

Table 1: Fixing p = 0.2 & Varying θ

θ	E(T) type (i)	E(H) type(i)	E(T) type(ii)	E(H) type(ii)
0.4	1.328810702	0.06828271	1.2625791	0.068177973
0.5	1.173963817	0.066117603	1.121890657	0.066126799
0.6	1.051345525	0.064406098	1.009340617	0.064487427
0.7	0.951855691	0.06301978	0.9172612	0.063147669

Table 2: Fixing θ = 0.4 & Varying p

p	E(T) type(i)	E(H) type(i)	E(T) type(ii)	E(H) type(ii)
0.2	1.328810702	0.06828271	1.26257191	0.068177973
0.4	1.344880091	0.069055767	1.292749454	0.06852013
0.6	1.360949481	0.069828824	1.322926999	0.068862286
0.8	1.37701887	0.070601882	1.353104542	0.069204443

(II) Simulation Studies:

(i) Simulation of Life Time of Organ A

In simulation studies, even two decimal places approximations for numbers are allowed and are sufficient but in this study higher (nine) decimal places approximations are considered since this study considers models on health problems and their treatment issues, higher decimal places approximations are at times more meaningful. The simulated values of the life times of organ A, organ B and the time to PT are required for the study. They are generated using the methods presented by Martin Haugh [9] by generating uniform random values u using Linear Congruential Generator (LCG). The random values for the life time of the organ A may be generated either using x_A=min {x : $F_A(x) \geq u$} or noting that the cyclic two-phase life time infinitesimal generator with starting phase 1of organ A may be replaced by (acyclic) Coxian-2 infinitesimal generator with starting phase 1 when corresponding Cdfs are equal. Using the arguments given for (15), (16) and (17) for the Cdf of time to PT, it may be noted that the following infinitesimal generator given by

$$Q'''=\begin{bmatrix} -(a+b) & a+b-\lambda_1 & \lambda_1 \\ 0 & -(a-b) & (a-b) \\ 0 & 0 & 0 \end{bmatrix} \quad (39)$$

which starts in (phase) level 1 has the absorption time distribution same as $F_A(x)$ given in (14) where a, b and $\lambda_1$are as defined for the life time of the organ A. This permits the replacement of the generator (1) of cyclic type by the generator (39) which is acyclic for studies since the Cdfs are equal. The Cdf $F_A(x)$ is Coxian-2 with parameters ((a + b), p'=$\frac{(a+b-\lambda_1)}{(a+b)}$, (a-b)) and with probability q'=1-p' for absorption from level 1 when the holding time is over in level 1 for organ A. There is no transition from level 2 to level 1 and (there is no loop-like) no cyclic formation of transitions from level 1 →level 2 → level l before absorptions. From level 2 absorption alone occurs after the holding time there. As in the numerical case-study the same values for the organ A transition rates are assumed with $\lambda_1 = 0.3, \lambda_2 = 0.35, \mu_1 = 0.4, \mu_2 = 0.5$. Then from (11), a=0. 775; b=0. 453458929; a + b=1. 228458929; a-b=0. 3215410713 and p'=0. 755791591 which gives the life time of organ A has Coxian-2 Cdf, F_A (t)=1-1. 02375195 $e^{-(0.3215410713)\,t}$+ 0. 02375195$e^{-(1.228458929)t}$ with pd f_A (t)=(0. 3291783) $e^{-(0.3215410713)\,t}$-(0. 0291783) $e^{-(1.228458929)t}$. The first and second exponential random time values of Coxian 2 random time part of life time of the organ A can be generated by

x'_A=-($\frac{1}{1.228458929}$)ln u and x''_A=-($\frac{1}{0.321541071}$) ln u (40)

where ln is natural logarithm and the random uniform values for the two are generated by two different LCGs.

Considering third uniform random value u generated by another LCG, the Coxian life time of the organ A becomes

$x_A = x'_A + x''_A$ if u ≤ p'=0. 755791591 and the Coxian time x_A becomes $x_A = x'_A$ if u > p'=0. 755791591. So the simulated random time values for life time of the organ A is

$$x_A = \begin{cases} x'_A + x''_A \; if \; u \leq p' = 0.755791591 \\ x'_A \; if \; u > p' = 0.755791591 \end{cases} \quad (41)$$

This shows for the life time of the organ A three random values are to be simulated by three different LCGs.

(ii) Simulation of Life Time of Organ B

In the numerical study the general life time of the organ B is assumed to follow an exponential distribution. When it has some unknown distribution the researcher has to fit the distribution of it using the data available (primary / secondary). The method is to find the first three moments from the data. When the first three moments are available it has been established that the EC distribution with parameter set $\left\{\tilde{p}, k, \theta, \theta_1, p_1, \theta_2\right\}$ where $1-\tilde{p}$ is the probability of non zero mass at time zero, for $0 < \tilde{p} \leq 1$ and with probability $\tilde{p}$ its distribution is the Cdf of the sum of Erlang (k, θ) and Coxian $(\theta_1, p_1, \theta_2)$ random variables is an excellent approximation for any general distribution function using the method of comparison of first three moments by T. Osogamy and M.H.Balter [8] where the details for finding the exact parameter values are also available. So the assumption and consideration of an EC distribution for the life time of the organ B is ideal for simulation studies. Further such a study with EC distribution is almost a study on any general distribution. Accordingly it is assumed that the organ B has EC life distribution with parameters set $\left\{\tilde{p}, k, \theta, \theta_1, p_1, \theta_2\right\}$ with respective values {1, 5, 2.5, 20, 0.5, 30} to study the Special case (2). Simulation study for the case of EC life distribution with $\tilde{p} < 1$ is similar. The method taken up here is valid for any set of values of the EC parameter set for the organ B. Since the life time of the organ B is the sum of Erlang and Coxian random times, its Erlang random time part is generated by

$$y = -\frac{1}{2.5} \ln \prod_{i=1}^{5} u_i \qquad (42)$$

where u_i are generated by different LCGs for i=1 to 5 and the two exponential random time values of Coxian random time part of the organ B are generated by

$$z = -\frac{1}{20} \ln u \text{ and } w = -\frac{1}{30} \ln u \qquad (43)$$

by two different LCGs. Considering third uniform random value u generated by another LCG, the Coxian time becomes z + w if $u \leq p_1 = 0.5$ and if $u > p_1 = 0.5$ the Coxian time becomes z . So the simulated random time values for the life time of the organ B is

$$x' = \begin{cases} y + z + w & if\ u \leq p_1 = 0.5 \\ y + z & if\ u > p_1 = 0.5 \end{cases} \qquad (44)$$

For the life time of the organ B eight random values are required to be simulated by eight different LCGs.

(iii) Simulation of Time to Prophylactic Treatment

Type (i) of Unequal Holding Rates $\alpha \neq \beta$

Let the parameters of the Coxian time to PT, (α, p, β) have values α=0. 5, p=0. 2, 0. 4, 0. 6, 0. 8 and β=1. Simulated uniform random values v', w' and v'' are required to decide the time to hospitalization for PT for its observation times and to decide whether second opinion is required. Observation times are simulated by considering

v'=-$\frac{1}{0.5}$ ln u, and v''=-$\frac{1}{1}$ ln u. (45)

The requirement of second observation is decided by w'. This gives the simulated time to PT for type (i) as

$$x''=\begin{cases} v' + v'' if\ w' \le p \\ v'\ if\ w' > p \end{cases} \quad (46)$$

Four values of p=0. 2, 0. 4, 0. 6 and 0. 8 are considered for the study. This makes for the simulation of time to PT, six uniform random values are to be simulated by six different LCGs two for α, β and four for p for type (i).

Type (ii) Equal Holding Rates α=β

Let the parameters of the Coxian time to PT, (α, p, β) have values for α=β=1 and p=0. 2, 0. 4, 0. 6, 0. 8. Simulated uniform random values v''', w'' and v'''' are required to decide the time to hospitalization for PT for its observation times and to decide whether second opinion is required. Observation times are simulated by considering

v'''=-$\frac{1}{1}$ ln u, and v''''=-$\frac{1}{1}$ ln u. (47)

The requirement of second observation is decided by w''. This gives the simulated time to prophylactic treatment is as follows for type (ii).

$$x'''=\begin{cases} v''' + v'''' if\ w'' \le p \\ v''' if\ w'' > p \end{cases} \quad (48)$$

One uniform random value is required to be simulated for the first observation time for α=1. For other random variables simulated values of type (i) for p and for the second exponential time may be used here. This makes for the simulation of time to PT for the types (i) and (ii) seven uniform random values are required to be simulated by six different LCGs for values of α, β and p for type (i) and by one LCG for α of type (ii).

(iv) Simulation of Time to Hospitalization

The simulated time to hospitalization for treatment is T=min {x_A, x', x''} for the type (i) and is T=min {x_A, x', x'''} for the type (ii). It may be noted that for the types (i) and (ii) 18 uniform random values three for the simulation of x_A, eight for the simulation of x', six for the simulations of x'' and one for the simulation of x''' are to be generated to simulate the time to hospitalization.

(v) Simulation of Hospital Treatment Time

In the parametric model one can assume the expected values of various treatment (hospitalization) times. Exact structures of the Cdf may not be required and the values of expectations alone are sufficient. Simulation studies are different. One has to study the types and stages of treatments as explained by Mark Fackrell [11] to get simulated hospital treatment times. Three types of treatments H_1 , $H_2 and\ H_3$ are considered. Let five, three and two stages of treatments one by one respectively for them be assumed as follows.

- Treatment H_1 : Emergency Department (ED) → Operation Theatre (OPT) → Intensive Care Unit (ICU) ↔ High Dependency Ward (HDW) → Ward (W) → Discharge

- Treatment H_2 : ED → ICU → W → Discharge and
- Treatment H_3 : ED → W→ Discharge.

In the treatment H_1 , loop like treatments, namely, ICU → HDW → ICU are also assumed to study the repetition of treatment at a stage. Let transitions from ED→OPT and OPT→ICU occur following exp(60). From ICU let the patient move to HDW in an exp(60). From HDW let the patient move to Ward W in an exp(60) or let the patient move back to ICU in an exp(40) so that the total holding time at HDW be exp(100). Let the holding time at W be exp(60) for the discharge of the patient. The infinitesimal generator 6 by 6 matrix with states for $H_1$is presented below.

$$Q''''=\begin{bmatrix} States & ED & OPT & ICU & HDW & W & D \\ ED & -60 & 60 & 0 & 0 & 0 & 0 \\ OPT & 0 & -60 & 60 & 0 & 0 & 0 \\ ICU & 0 & 0 & -60 & 60 & 0 & 0 \\ HDW & 0 & 0 & 40 & -100 & 60 & 0 \\ W & 0 & 0 & 0 & 0 & -60 & 60 \\ D & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}.$$

The sub matrix Q^v of the matrix Q'''' with the cyclic formation is

$$Q^v = \begin{bmatrix} States & ICU & HDW & W \\ ICW & -60 & 60 & 0 \\ HDW & 40 & -100 & 60 \end{bmatrix}.$$

This may be compared with cyclic Q in (1) which has been replaced by acyclic Q''' in (39). Using (39) and taking $\lambda_1 = 0$, $\lambda_2 = 60, \mu_1 = 60, \mu_2 = 40$, it can be seen that a=80, b=52. 9150262213, a + b=132. 9150262213=c (say), a-b=27. 0849737787=d (say) (49)

the sub matrix Q^v gets the replacement by $\begin{bmatrix} -c & c & 0 \\ 0 & -d & d \end{bmatrix}$. Replacing this for Q^v in Q'''' the acyclic infinitesimal generator obtained for treatment $H_1$is seen as below.

$$Q^{vi} = \begin{bmatrix} States & ED & OPT & ICU & HDW & W & D \\ ED & -60 & 60 & 0 & 0 & 0 & 0 \\ OPT & 0 & -60 & 60 & 0 & 0 & 0 \\ ICU & 0 & 0 & -c & c & 0 & 0 \\ HDW & 0 & 0 & 0 & -d & d & 0 \\ W & 0 & 0 & 0 & 0 & -60 & 60 \\ D & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \quad (50)$$

The random hospitalization times H_2 and H_3 are assumed to have Erlang distributions E(3, 60) and E(2, 60) respectively. Assuming the treatment patterns are same for the two types (i) and (ii), it may be noted that the simulated hospitalization times for treatments H_1, H_2 and H_3 are respectively H_1=-($\frac{1}{60}$) ln $\prod_{i=1}^{3} u_i - (\frac{1}{c})$ ln $u_5 - (\frac{1}{d})u_6$; H_2=-($\frac{1}{60}$) ln $\prod_{i=1}^{3} u_i$ and H_3=-($\frac{1}{60}$)ln $\prod_{i=1}^{2} u_i$. (51)

The random values u_i appearing on the right side of H_j for j=1, 2, 3 are to be generated by ten different LCGs for various values of i. It may be noted that 10 random variables are considered for hospital treatment times, namely, 5 random variables with exponential distribution for H_1; 3 random variables with exponential distributions for H_2; 2 random variables with exponential distributions for H_3.

(vi) Generating Random Values Using LCG

The total number of uniform random values for the two types (i) and (ii) are 28, namely, 18 for the time to hospitalization and 10 for hospital treatment times. These 28 uniform random u_i for i=1 to 28 values are generated by linear congruential generators Z_{n+1}=(a$Z_n + c$)mod 16 with seed value Z_0 whose short form representation is given by LCG (a, c, 16, Z_0) for different values of a, c and Z_0. This generates all the sixteen remainder values of division by 16 in random manner so that sixteen uniform random values u=$\frac{z}{16}$ given by {0. 0625, 0. 375, 0. 9375, 0. 75, 0. 8125, 0. 125, 0. 6875, 0. 5, 0. 5625, 0. 875, 0. 4375, 0. 25, 0. 3125, 0. 625, 0. 1875, 0}are obtained in some order. It may be noted that for uniform distribution E(U)=. 5 and Variance=1/12=. 08333. They are comparable with average simulated value 0. 46875 and its variance 0. 083 of the data. The value u=0 in the above gives extreme value of the simulated random value since natural logarithm of u, namely, ln (u) is required for simulation. When u=0 is deleted the average becomes. 5 equal to E(U). The LCGs used for the Special case(2) are listed here.

- For simulation of the life time of the organ A, the LCG (5, 1, 16, 1), LCG(9, 1, 16, 2) and LCG(13, 1, 16, 3) are used.
- For organ B the following LCGs are used as follows. Erlang with phase 5 and parameter 2. 5 life part of the organ B, LCG(1, 3, 16, 4), LCG(5, 3, 16, 5), LCG(9, 3, 16, 6), LCG(13, 3, 16, 7) and LCG(1, 5, 16, 8) are used; for the Coxian life part with parameter 20 of exponential time of the organ B, LCG(5, 5, 16, 9) is used; LCG (9, 5, 16, 10) is used for the probability p_1=0. 5 to decide the occurrence of the second exponential treatment time and LCG(13, 5, 16, 11) is used for the second Coxian exponential time with parameter 30.
- For the type (i) of the PT, six LCGs are used, namely, LCG(1, 7, 16, 12) for the parameter α=0. 5 of the first exponential time, LCG(5, 7, 16, 13), LCG(9, 7, 16, 14), LCG(13, 7, 16, 15) and LCG(1, 9, 16, 1) for the probability p=0. 2, 0. 4, 0. 6, 0. 8 and LCG(5, 9, 16, 2) for the parameter β=1 of the second exponential time.
- For the type (ii) of the PT, one LCG is used, namely, LCG(9, 9, 16, 3), for the parameter α=1 of the first exponential time, as type (ii) differs from type (i) in that part only so that other simulated values of p and β of type (i) can be used.
- For the first and second exponential times of hospitalization time of H_1, LCG(13, 9, 16, 4) and LCG(1, 11, 16, 5) are used; for the acyclic first and second exponentials parts LCG(5, 11, 16, 6) and LCG(9, 11, 16, 7) are used and for the last exponential time LCG(13, 11, 16, 8) is used.
- For the Erlang phase 3 hospitalization time of H_2, LCG(1, 13, 16, 9), LCG(5, 13, 16, 10), and LCG(9, 13, 16, 11) are used.
- For the Erlang phase 2 hospitalization time of H_3, LCG(13, 13, 16, 12) and LCG(1, 15, 16, 13) are used.

All the 28 LCGs used above namely, the LCG (a, c, m, Z_0) for a=1, 5, 9, 13; c=1, 3, 5, 7, 9, 11, 13, 15; m=16 ; Z_0=1 to 15 have full period of length 16. The values of a, c mentioned here with Z_0=1 to 15 and m=16 satisfy the Hull and Dobell theorem [10] which guarantees the LCGs to have full period.

(vii)Results for Special case (2):
The following table 3 gives the failure times of the organ A in fifth column. Exponential random times are simulated using inverse method described earlier. The Organ A failure time is simulated using (40) and (41). They are presented in red color. The second simulated value in column 4 is added to the first simulated value in column 2 when u value in column 3 is u ≤ p'=0. 755791591 marked in red color. Sim indicates simulation.

Table 3: Life Time of Organ A

Organ A	a + b=1.228458929	U for p'=0.755791591	a-b=0.3215410713	Life time of organ A
Sim 1	2.256964931	**0.125**	5.206104548	**7.463069479**
Sim 2	0.798422503	**0.1875**	2.1557034	**2.954125903**
Sim 3	0.052536165	**0.75**	1.789395496	**1.841931662**
Sim 4	0.23418127	**0.8125**	3.050401148	**0.23418127**
Sim 5	0.169024263	**0.375**	0.20071626	**0.369740522**
Sim 6	1.692723698	**0.4375**	4.311406799	**6.004130498**
Sim 7	0.30501097	**0.0625**	3.617425311	**3.922436281**
Sim 8	0.564241233	**0.625**	6.467110199	**7.031351432**
Sim 9	0.468362541	**0.6875**	1.165305097	**1.633667638**
Sim 10	0.108698296	**0.25**	8.622813599	**8.731511895**
Sim 11	0.672939529	**0.3125**	0.415285649	**1.088225179**
Sim 12	1.128482466	**0.875**	2.570989049	**1.128482466**
Sim13	0.94683736	**0.9375**	0.894697748	**0.94683736**
Sim 14	0.382596128	**0.5**	0.645763118	**1.028359246**
Sim 15	1.362663736	**0.5625**	1.461721911	**2.824385647**

Failure time of the Organ B is given in green color in table 4 column 6 using the equations in (42), (43) and (44). Coxian simulated second exponential time in column 5 of table 4 is to be added with the sum of terms of second and third columns when u value for p_1 is u ≤ 0. 5 which is marked in green color in column 4. The minimum of the life time of the organ A (listed in table 3 column 5) and of the life time of the organ B (presented in column 6 table 4) is presented in column 7 with red and green color to indicate the failure time of organ A and organ B respectively

Table 4: Life Time of Organ B

	Erlang(5, 2.5)	Coxian Exp 1	U for p_1=0.5	Coxian Exp 2	Life time of B	Min(A, B)
Sim 1	2.020040071	0.028768207	**0.625**	0.012489782	**2.048808278**	**2.048808278**
Sim 2	0.812358219	0.103972077	0.9375	0.046209812	**0.916330296**	**0.916330296**
Sim 3	1.830256879	0.003226926	0.75	0.019178805	**1.833483805**	**1.833483805**
Sim 4	1.075070034	0.05815754	0.0625	0.015666788	**1.148894362**	**0.23418127**
Sim 5	1.996463057	0.00667657	0.875	0.027555952	**2.003139626**	**0.369740522**
Sim 6	3.467994704	0.018734672	0.1875	0.038771694	**3.52550107**	**3.52550107**
Sim 7	2.206900295	0.014384104	0.3125	0.032694308	**2.253978707**	**2.253978707**

Sim 8	0.516491341	0.138629436	0.125	0.055799214	**0.710919991**	0.710919991
Sim 9	2.180444374	0.023500181	0.4375	0.009589402	**2.213533958**	1.633667638
Sim10	1.857854028	0.041333929	0.25	0.092419624	**1.991607581**	1.991607581
Sim 11	2.018258331	0.034657359	0.5625	0.069314718	**2.05291569**	1.088225179
Sim 12	2.798404131	0.010381968	0.375	0.002151284	**2.810937383**	1.128482466
Sim 13	0.928339108	0.049041463	0.6875	0.023104906	**0.97738057**	0.946837336
Sim 14	0.99922169	0.083698822	0.5	0.006921312	**1.089841824**	1.028359246
Sim 15	2.671022638	0.069314718	0.8125	0.004451046	**2.740337356**	2.740337356

Coxian exponential times 1 and 2 are presented in columns 2 and 7 of table 5 for the time to PT of the type (i) when α=0. 5 $\neq$ β=1 using (45) and (46). The column 7, which is the second observation time, is considered for addition when u values in the columns 3 to 6 are not greater than p=0. 2, 0. 4, 0. 6, 0. 8 by **purple** color. Using table 5, simulated times for PT are presented in table 6 considering addition where ever second observations are required for type (i) in the columns 2 to 4. Simulated time to hospitalization T is presented below in table 6 for α=0. 5 and β=1. In all the tables presented hereafter the **Red color** indicates the patient is admitted due to the organ A failure; the **green color** indicates he is admitted due to the organ B failure and **the purple color** indicates he is admitted for PT respectively for various p values. From table 6 one can find the average values of T for type (i). Coxian exponential times 1 and 2 are presented in columns 2 and 7 of table 7 for the time to PT of the type (ii) when α=β=1 using (47) and (48). The column 7 is considered for addition when u values in the columns 3 to 6 are not greater than p=0. 2, 0. 4, 0. 6 and 0. 8 by **purple** color respectively.

Table 5: Simulated Random Values for Components of Time to Prophylactic Treatment for Type (i)

α=0.5, β=1	Cox 1 (para0.5)	U for p=0.2	U for p=0.4	U for p=0.6	U for p=0.8	Cox 2 (para 1)
Sim 1	0.575364145	**0.8125**	**0.875**	**0.9375**	**0.0625**	2.079441542
Sim 2	3.347952867	**0.5**	**0.3125**	**0.625**	**0.625**	1.673976434
Sim 3	0.940007258	**0.9375**	**0.25**	**0.5625**	**0.1875**	0.693147181
Sim 4	5.545177444	**0.125**	**0.6875**	**0.75**	**0.75**	2.772588722
Sim 5	1.386294361	**0.0625**	**0.625**	**0.1875**	**0.3125**	0.133531393
Sim 6	0.129077042	**0.75**	**0.0625**	**0.875**	**0.875**	0.064538521
Sim 7	1.961658506	**0.1875**	**0.4375**	**0.8125**	**0.4375**	1.386294361
Sim 8	0.41527873	**0.375**	**0.375**	**0.4375**	**0.5625**	0.207639365
Sim 9	2.772588722	**0.3125**	**0.8125**	**0.125**	**0.125**	0.470003629
Sim 10	0.749386899	**0.4375**	**0.75**	**0.0625**	**0.6875**	0.374693449
Sim 11	4.158883083	**0.625**	**0.1875**	**0.25**	**0.25**	0.575364145
Sim 12	1.15072829	**0.5625**	**0.125**	**0.6875**	**0.8125**	0.980829253
Sim 13	1.653357146	**0.25**	**0.5625**	**0.375**	**0.375**	0.826678573
Sim 14	0.267062785	**0.6875**	**0.5**	**0.3125**	**0.9375**	0.287682072
Sim 15	2.32630162	**0.875**	**0.9375**	**0.5**	**0.5**	1.16315081

Table 6: Simulated Times of Prophylactic Treatment (PT) and Hospitalization (T) for (α, β)=(0. 5, 1) for p

	PT for p=0.2	PT for p=0.4	PT for p=0.6	PT for p=0.8	T for P=0.2	T for p=0.4	T for p=0.6	T for p=0.8
Sim 1	**0.575364145**	**0.575364145**	**0.575364145**	**2.654805687**	**0.575364145**	**0.575364145**	**0.575364145**	**2.048808278**
Sim 2	**3.347952867**	**5.021929301**	**3.347952867**	**5.021929301**	**0.916330296**	**0.916330296**	**0.916330296**	**0.916330296**
Sim 3	**0.940007258**	**1.633154439**	**0.940007258**	**0.940007258**	**0.940007258**	**1.633154439**	**0.940007258**	**0.940007258**
Sim 4	**8.317766167**	**5.545177444**	**5.545177444**	**8.317766167**	**0.23418127**	**0.23418127**	**0.23418127**	**0.23418127**
Sim 5	**1.519825754**	**1.386294361**	**1.519825754**	**1.519825754**	**0.369740522**	**0.369740522**	**0.369740522**	**0.369740522**
Sim 6	**0.129077042**	**0.129077042**	**0.129077042**	**0.193615563**	**0.129077042**	**0.129077042**	**0.129077042**	**0.193615563**
Sim 7	**3.347952867**	**1.961658506**	**1.961658506**	**3.347952867**	**2.253978707**	**1.961658506**	**1.961658506**	**2.253978707**
Sim 8	**0.41527873**	**0.622918094**	**0.622918094**	**0.622918094**	**0.41527873**	**0.622918094**	**0.622918094**	**0.622918094**
Sim 9	**2.772588722**	**2.772588722**	**3.242592351**	**3.242592351**	**1.633667638**	**1.633667638**	**1.633667638**	**1.633667638**
Sim 10	**0.749386899**	**0.749386899**	**1.124080348**	**1.124080348**	**0.749386899**	**0.749386899**	**1.124080348**	**1.124080348**
Sim 11	**4.158883083**	**4.734247228**	**4.734247228**	**4.734247228**	**1.088225179**	**1.088225179**	**1.088225179**	**1.088225179**
Sim 12	**1.15072829**	**2.131557543**	**1.15072829**	**1.15072829**	**1.128482466**	**1.128482466**	**1.128482466**	**1.128482466**
Sim13	**1.653357146**	**1.653357146**	**2.48003572**	**2.48003572**	**0.94683736**	**0.94683736**	**0.94683736**	**0.94683736**
Sim 14	**0.267062785**	**0.267062785**	**0.554744858**	**0.267062785**	**0.267062785**	**0.267062785**	**0.554744858**	**0.267062785**
Sim 15	**2.32630162**	**2.32630162**	**3.489452429**	**3.489452429**	**2.32630162**	**2.32630162**	**2.740337356**	**2.740337356**

Table 7: Simulated Values for the Components of Time to Prophylactic Treatment for Type (ii)

α=1, β=1	Cox 1 (para 1)	U for p=0.2	U for p=0.4	U for p=0.6	U for p=0.8	Cox 2 (para 1)
Sim 1	1.673976434	0.8125	0.875	0.9375	**0.0625**	2.079441542
Sim 2	1.386294361	0.5	**0.3125**	0.625	**0.625**	1.673976434
Sim 3	0.207639365	0.9375	**0.25**	**0.5625**	**0.1875**	0.693147181
Sim 4	0.133531393	**0.125**	0.6875	0.75	**0.75**	2.772588722
Sim 5	0.826678573	**0.0625**	0.625	**0.1875**	**0.3125**	0.133531393
Sim 6	0.693147181	0.75	**0.0625**	0.875	0.875	0.064538521
Sim 7	2.772588722	**0.1875**	0.4375	0.8125	**0.4375**	1.386294361
Sim 8	2.079441542	0.375	**0.375**	**0.4375**	**0.5625**	0.207639365
Sim 9	0.374693449	0.3125	0.8125	**0.125**	**0.125**	0.470003629
Sim 10	0.287682072	0.4375	0.75	**0.0625**	**0.6875**	0.374693449
Sim 11	1.16315081	0.625	**0.1875**	**0.25**	**0.25**	0.575364145
Sim 12	0.980829253	0.5625	**0.125**	0.6875	0.8125	0.980829253
Sim 13	0.064538521	0.25	0.5625	**0.375**	**0.375**	0.826678573
Sim 14	0.575364145	0.6875	0.5	**0.3125**	0.9375	0.287682072
Sim 15	0.470003629	0.875	0.9375	**0.5**	**0.5**	1.16315081

Using table 7, simulated times for PT are presented in table 8 considering addition where ever second observations are required for type (ii). Time to hospitalization T is presented below for α=1=β in table 8 in columns 6 to 8. The hospital treatment times may be simulated as follows. The treatment time $H_1$is the sum of Erlang random variable with parameter set (2, 60) and three exponential random variables with parameters c, d and 60 where c and d are given by (49). The simulated components of $H_1$are given below in table 9 in columns 2 to 5. The total treatment time for H_1 is given in column 6 table 9 by adding the columns 2 to 6 of table 9. The treatment times H_2 and H_3 are generated by LCGs as mentioned in (vi) earlier. The simulated values

in table 9 are common for the two types (i) and (ii). They are to be linked to columns 6 to 9 of table 6 and table 8 for the types (i) and (ii). For example in simulation 4 for p=0. 2 in table 6 the organ A fails at time **0. 23418127** and his hospital treatment time for $H_1$is to be **0. 131681178.** For the fifteen simulations in table 6 for various values of p the corresponding treatment types and times are listed in table 10 for the type (i) in columns 2 to 5. The simulated values of table 8 are to be linked to table 9 for type (ii). For example in table 8 simulation 8 for p=0. 2, the patient is admitted for hospitalization due to the failure of the organ B at time **0. 710919991** and he is to be provided treatment H_2 for time **0. 1203192313** which is placed in table 10 simulation 8 column 6. In a similar manner all the fifteen simulations of table 8 for various values of p may be linked with corresponding simulated treatment times in table 9. They are presented in table 10 for type (ii) in columns 6 to 9.

Table 8: Simulated Times for Prophylactic Treatment (PT) and Hospitalization (T) for (α, β)=(1, 1) for p

	PT for p=0.2	**PT for p=0.4**	**PT for p=0.6**	**PT for p=0.8**	**T for p=0.2**	**T for p=0.4**	**T for p=0.6**	**T for p=0.8**
Sim 1	**1.673976434**	**1.673976434**	**1.673976434**	**3.753417975**	**1.673976434**	**1.673976434**	**1.673976434**	**2.048808278**
Sim 2	**1.386294361**	**3.060270795**	**1.386294361**	**3.060270795**	**0.916330296**	**0.916330296**	**0.916330296**	**0.916330296**
Sim 3	**0.207639365**	**0.900786545**	**0.900786545**	**0.900786545**	**0.207639365**	**0.900786545**	**0.900786545**	**0.900786545**
Sim 4	**2.906120115**	**0.133531393**	**0.133531393**	**2.906120115**	**0.23418127**	**0.133531393**	**0.133531393**	**0.23418127**
Sim5	**0.960209966**	**0.826678573**	**0.960209966**	**0.960209966**	**0.369740522**	**0.369740522**	**0.369740522**	**0.369740522**
Sim 6	**0.693147181**	**0.757685702**	**0.693147181**	**0.693147181**	**0.693147181**	**0.757685702**	**0.693147181**	**0.693147181**
Sim 7	**4.158883083**	**2.772588722**	**2.772588722**	**4.158883083**	**2.253978707**	**2.253978707**	**2.253978707**	**2.253978707**
Sim 8	**2.079441542**	**2.287080906**	**2.287080906**	**2.287080906**	**0.710919991**	**0.710919991**	**0.710919991**	**0.710919991**
Sim 9	**0.374693449**	**0.374693449**	**0.844697079**	**0.844697079**	**0.374693449**	**0.374693449**	**0.844697079**	**0.844697079**
Sim10	**0.287682072**	**0.287682072**	**0.662375522**	**0.662375522**	**0.287682072**	**0.287682072**	**0.662375522**	**0.662375522**
Sim11	**1.16315081**	**1.738514955**	**1.738514955**	**1.738514955**	**1.088225179**	**1.088225179**	**1.088225179**	**1.088225179**
Sim12	**0.980829253**	**1.961658506**	**0.980829253**	**0.980829253**	**0.980829253**	**1.128482466**	**0.980829253**	**0.980829253**
Sim13	**0.064538521**	**0.064538521**	**0.891217094**	**0.891217094**	**0.064538521**	**0.064538521**	**0.891217094**	**0.891217094**
Sim14	**0.575364145**	**0.575364145**	**0.863046217**	**0.575364145**	**0.575364145**	**0.575364145**	**0.863046217**	**0.575364145**
Sim 15	**0.470003629**	**0.470003629**	**1.633154439**	**1.633154439**	**0.470003629**	**0.470003629**	**1.633154439**	**1.633154439**

Table 9: Hospital Treatment Times for Stage for Type $H_1$and Treatment Times for $H_1, H_2 and\ H_3$

	H1 Erlang (2, 60)	H1 exp(c)	H1 exp(d)	H1 exp(60)	**H1 Total time**	**H2 Erlang (3, 60)**	**H3 Erlang (2, 60)**
Sim1	0.042490753	0.007379371	0.030521668	0.011552453	**0.091944244**	**0.023667687**	**0.008255357**
Sim 2	0.009705547	0.004328812	0.017352929	0.027899607	**0.059286895**	**0.020883452**	**0.014384104**
Sim 3	0.051004513	0.005214965	0.042944506	0.034657359	**0.133821343**	**0.074109419**	**0.04090225**
Sim 4	0.074109419	0.012594336	0.025591577	0.019385847	**0.131681178**	**0.023922145**	**0.02161137**
Sim 5	0.014384104	0.003536121	0.061804617	0.004794701	**0.084519543**	**0.047285454**	**0.021141855**
Sim 6	0.016003499	0.001562196	0.036213041	0.013777976	**0.067556712**	**0.066232679**	**0.0309383**
Sim 7	0.035733001	0.002164406	0.102366306	0.016347154	**0.156610868**	**0.062556966**	**0.016003499**
Sim 8	0.008255357	0.006219602	0.051183153	0.009589402	**0.075247515**	**0.120319231**	**0.044246761**
Sim 9	0.0309383	0.001004637	0.002382816	0.006244891	**0.040570644**	**0.048435335**	**0.042490753**
Sim 10	0.035733001	0.020859859	0.07677473	0.007833394	**0.141200984**	**0.039408714**	**0.069314718**
Sim11	0.008470414	0.002819045	0.00766622	0.003460656	**0.022416335**	**0.022846503**	**0.035733001**
Sim 12	0.021141855	0.015644894	0.013833997	0.023104906	**0.073725653**	**0.035389346**	**0.035733001**
Sim 13	0.069314718	0.008751086	0.004930091	0.001075642	**0.084071537**	**0.067351667**	**0.049670468**
Sim 14	0.017422796	0.01042993	0.021242928	0.002225523	**0.051321177**	**0.015459746**	**0.017422796**
Sim 15	0.02161137	0.000485562	0.010621464	0.046209812	**0.078928208**	**0.016609627**	**0.008470414**

Table 10 : Hospital Treatment times H for Type (i) Rates (α, β)=(0. 5, 1) & Type (ii) Rates (α, β)=(1, 1)

	H time p=0.2	H time p=0.4	H time p=0.6	H time p=0.8	H time p=0.2	H time p=0.4	H time p=0.6	H time p=0.8
Sim1	0.008255357	0.008255357	0.008255357	0.023667687	0.008255357	0.008255357	0.008255357	0.023667687
Sim 2	0.020883452	0.020883452	0.020883452	0.020883452	0.020883452	0.020883452	0.020883452	0.020883452
Sim 3	0.04090225	0.04090225	0.04090225	0.04090225	0.04090225	0.04090225	0.04090225	0.04090225
Sim 4	0.131681178	0.131681178	0.131681178	0.131681178	0.131681178	0.131681178	0.131681178	0.131681178
Sim 5	0.084519543	0.084519543	0.084519543	0.084519543	0.084519543	0.084519543	0.084519543	0.084519543
Sim 6	0.0309383	0.0309383	0.0309383	0.0309383	0.0309383	0.0309383	0.0309383	0.0309383
Sim 7	0.062556966	0.016003499	0.016003499	0.062556966	0.062556966	0.062556966	0.062556966	0.062556966
Sim 8	0.044246761	0.044246761	0.044246761	0.044246761	0.120319231	0.120319231	0.120319231	0.120319231
Sim 9	0.040570644	0.040570644	0.040570644	0.040570644	0.042490753	0.042490753	0.042490753	0.042490753
Sim 10	0.069314718	0.069314718	0.069314718	0.069314718	0.069314718	0.069314718	0.069314718	0.069314718
Sim 11	0.022416335	0.022416335	0.022416335	0.022416335	0.022416335	0.022416335	0.022416335	0.022416335
Sim 12	0.073725653	0.073725653	0.073725653	0.073725653	0.035733001	0.073725653	0.035733001	0.035733001
Sim 13	0.084071537	0.084071537	0.084071537	0.084071537	0.049670468	0.049670468	0.049670468	0.049670468
Sim 14	0.017422796	0.017422796	0.017422796	0.017422796	0.017422796	0.017422796	0.017422796	0.017422796
Sim 15	0.008470414	0.008470414	0.016609627	0.016609627	0.008470414	0.008470414	0.008470414	0.008470414

The average values of simulated T and H for types (i) and (ii) (listed in tables (6), (8) and (10)) are presented in table (11). Figures 1 and 2 present the averages for various values of p. Figure 1 and figure 2 present the effect of p on the average of simulated values of T and H for various values of p for the two types. In the type (i) and type (ii) the only difference is in the value of α where in type (i) α=0. 5 and in type (ii) α=1. The effect of the change of α may be seen on comparing figures (1) and (2) for averages.

Table 11: Averages of T and H for Type (i) and Type (ii) for values of p

Special Case (2) p□=1	p=0.2	p=0.4	p=0.6	p=0.8
Average of T for (0.5, 1)	0.931594795	0.972159217	0.997710156	1.100551542
Average of H for (0.5, 1)	0.049331727	0.046228163	0.046770777	0.05090183
Average of T for (1, 1)	0.726750001	0.780395937	0.974397057	0.986917033
Average of H for (1, 1)	0.049704984	0.052237828	0.049704984	0.050732473

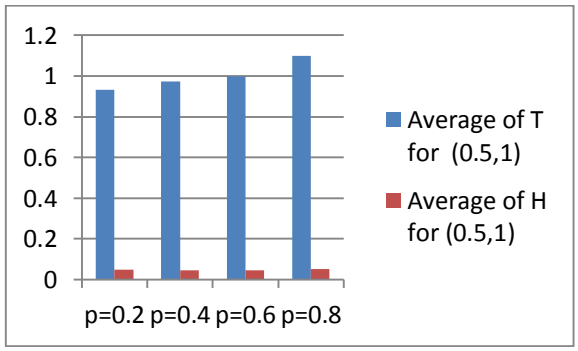

Figure 1: Averages of T and H: α=0. 5 & β=1.

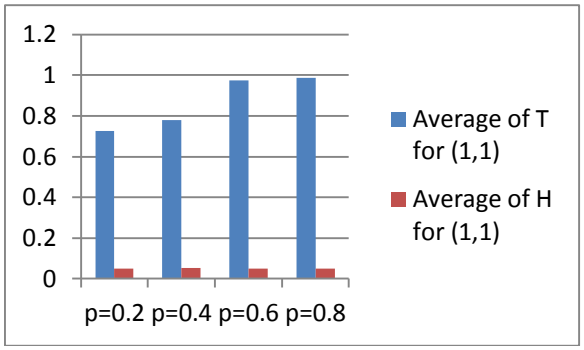

Figure 2: Averages of T and H: α=1 & β=1

Conclusion

Diabetic models with two observation times including one for second opinion for prophylactic treatment have been studied with two defective organs. Two types have come up depending on the observation holding rates are equal or not equal. Here the patient is sent for hospitalization when an organ fails out of two defective organs or when prophylactic treatment starts. The organ A of the patient has two phase PH life time distribution and his organ B has general life time. The time to prophylactic treatment has Coxian 2 distribution. The hospitalization times for the organ A, for the organ B and for prophylactic treatments have distinct distributions. The joint transform of the joint distribution of time to hospitalization and hospitalization time are obtained. Individual distributions, and their expected times are derived. Numerical studies are presented for the two types. Simulation study is taken up considering (i) the phase 2 life time distribution for the organ A, (ii) EC distribution of the life time for the organ B, (iii) Coxian time to prophylactic treatment and (iv) Erlang and cyclic phase type distributions for hospitalization times for the two types. Cyclic phase 2 type infinitesimal generator is replaced by acyclic phase 2 type by using equality of the distributions. Since not much of simulation analysis are available in literature for diabetic models, this paper opens up a real life like study.

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